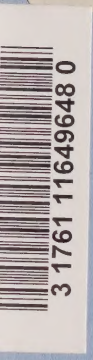

ROYAL COMMISSION ON MATTERS OF HEALTH AND SAFETY

ARISING FROM THE USE OF ASBESTOS IN ONTARIO

CHAIRMAN: J. STEFAN DUPRE, Ph.D.

COMMISSIONERS: J. FRASER MUSTARD, M.D.

ROBERT UFFEN, Ph.D., P.Eng., F.R.S.C.

COUNSEL: JOHN I. LASKIN

APPEARANCES: P. Casgrain, Quebec Asbestos Mining Association

L. Jolley, Ontario Federation of Labour

T. Hardy, Asbestos Information Association of North America

J. McNamee, Government of Ontario

Mr. Schumaher, Government of Ontario

180 Dundas Street
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VOLUME XXVIII

ROYAL COMMISSION ON MATTERS OF HEALTH AND SAFETY

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Volume XXVIII

THE FURTHER PROCEEDINGS OF THIS INQUIRY RESUMED PURSUANT TO ADJOURNMENT

APPEARANCES AS HERETOFORE NOTED

DR. DUPRE: Good morning, ladies and gentlemen.

M. Casgrain, it is my understanding that you will conduct the direct examination of Professor Dunnigan?

M. CASGRAIN: Yes, sir.

DR. DUPRE: Counsel, are there any announcements you wish to make before I greet the witness?

MR. LASKIN: No, Mr. Chairman, there are not.

DR. DUPRE: Do the parties have any points to raise?

(REPORTER'S NOTE: The chairman greeted the witness in French.)

DR. DUPRE: Miss Kahn, will you swear in the witness, please?

JACQUES DUNNIGAN, SWORN

EXAMINATION-IN-CHIEF BY M. CASGRAIN

DR. DUPRE: Proceed, counsel.

M. CASGRAIN: Mr. Chairman, I have just handed to yourself and to the other participants the paper that Dr. Dunnigan

M. CASGRAIN: (cont'd.) will be presenting in due course, which will be part of his expose, although he will also deal with the paper that you have had occasion to see which is the article, being a reprint from the Fourth International Conference on Asbestos.

M. CASGRAIN: Q. Dr. Dunnigan, you have handed to me, but you have not made a copy of it, your curriculum vitae, so perhaps we could go through your curriculum vitae quickly to establish your credentials, and perhaps in due course, Miss Kahn, you will wish to copy this and hand it over to the members of the panel.

Dr. Dunnigan, I understand that, from your curriculum vitae that you hold a B.A. from University of Montreal in 1956, that you have a B.Sc. with Honors from University of Ottawa in 1960, and that you have a Ph.D. in biology from University of Ottawa in 1963?

THE WITNESS: A. That is right.

Q. I understand as well that you have post-doctoral studies at Laval University in biochemistry, and that you held a number of posts including professor adjoint in biology at University of Sherbrooke; aggregate professor University of Sherbrooke; vice-dean of research, faculty of science, University of Sherbrook; and vice-recteur or vice-rector in research University of Sherbrooke.

In 1979, if I understand correctly, you were the one who set up the research program at the University of Sherbrooke on asbestos, and finally in 1980, you were appointed director general of the Institut de Recherche et de development sur l'amiante, otherwise known as IRDA, I R D A.

Is that correct?

A. That is correct, sir.

Q. I understand as well that you have participated in and written a number of papers, the list of which is before us. It is about five pages, two of which in particular deal with asbestos - namely, Cytotoxic and Haemolytic Effects of Native and Chemically-modified Chrysotile, at the Fifth International Conference in Turino, and also another paper on the Haemolytic Activity of Chrysotile Asbestos Fibers: A Freeze-fracture Study.

This is in addition to other writings that you have delivered on other matters as well.

Having said this, I presume that your specialty is biology?

A. Yes.

Q. You have given us, some time ago, this extract from the Fourth International Conference on Asbestos, which is entitled, Cytotoxic and Haemolytic Effect of Native and Chemically-modified Chrysotile, and you have also allowed me to produce this expose that I just handed to the panel.

Do I understand correctly, Dr. Dunnigan, that today you propose to speak to us mostly in respect of item four of the mandate of this committee, namely other asbestos exposure, and more specifically, on the use of asbestos products, safe use thereof. Is that correct?

A. That is correct, sir.

Q. To that end, however, you have produced this paper, you have given out this paper on the modification of chrysotile, biological and chemical modification of chrysotile, and will you perhaps say that this is so as to give us a background on the rest of the expose that you propose to give us, is that correct?

A. Yes, sir.

Q. Perhaps, Dr. Dunnigan, we could ask you to

Q. (cont'd.) summarize that paper which you wrote jointly with Dr. Nadeau, Dr. Paradis, Dr. Pele, Calvert, Lalancette and Cossette, which we have before us. Could you please do that?

A. Mr. President, what I intend to do with this paper, I will try not to summarize the whole paper, because this is not the object of my presentation. The object of my presentation is the document that you have before you, but I will try to extract from that paper which we gave in Torino, what is pertinent to that particular paper you have in front of you, because I think that some of these things which were given in that paper lead us naturally...it is in the same line of thought and it will lead us naturally to that particular paper.

Now, in that paper, which was given in May, 1980, in Torino, we presented preliminary data that we had obtained at the time on the effects of the various treatments, various chemical treatments or physical treatments of fibers.

Such treatments were treatment with acid, treatment with heat, and various chemical treatments with some compounds, and especially a phosphate treatment.

Now, the exact nature of this particular phosphate treatment could not be disclosed at the time, and you will understand why. It was because it was felt that this particular treatment could be a great potential, industrial potential, for treating chrysotile fibers and therefore no detail of the procedure should be disclosed at that time, until a proper patent protection will be made.

This has now been carried through, and I understand that the patenting process is, I think, one hundred percent completed and the full disclosure of the particular way of that phosphate is given, will be made public, because the industrial protection is now made.

THE WITNESS: (cnt'd.) But even then at that time, it was felt that there was in the world...when I say the world I mean data from France, from U.K., from South Africa, and we will go quickly over these...it was felt that there was a sufficiently large body of data that...not only ours...but pointing to the possibility that chemical characteristics of the fibers could play an important role in the biological effect ascribed to chrysotile fibers.

To my knowledge, evidence supporting that...let's call it chemical hypothesis...started to accumulate from the late sixties and early seventies. Part of it is reported in the introduction of that paper.

With your permission, we will go over these data which are reported in the first page of that paper given in Torino.

M. CASGRAIN: Q. One moment, Mr. Dunnigan. When you refer to 'that paper', perhaps, Mr. Chairman, we could give an exhibit number to the paper so that later on we could refer to it.

Since we have produced this expose of Mr. Dunnigan in a binder form which contains eight tabs, perhaps the best way to do it would be to call that paper tab number nine so it would follow naturally from this one.

Does that make sense?

MR. LASKIN: Yes. Exhibit forty.

M. CASGRAIN: So it will be exhibit forty, tab nine that you are now referring to, Dr. Dunnigan, tab nine being Cytotoxic and Haemolytic Effect of Native and Chemically-Modified Chrysotile.

EXHIBIT # 40: The abovementioned documents were then produced and marked.

THE WITNESS: A. All right. Now, if you take exhibit forty, tab nine, first page, second paragraph, we will

THE WITNESS: (cont'd.) run quickly over these data which I have mentioned, which are in line, which are in agreement with a chemical, so to speak, explanation of the biological properties of asbestos fibers.

In the late sixties and early seventies, Harington and Allison's work - these were published in 1973, you will find this in the references of this tab nine - did point to the possibility that at least part of the biological effects could be associated with some chemical - I say some - chemical surface characteristics of chrysotile. These authors showed some correlation between on the one hand what is called hemolytic activity or hemolytic potency, and also macrophage cytolytic potency on the one hand, and the concentration of magnesium on the surface of asbestos fibers.

Further evidence...

Q. Dr. Dunnigan, before going on I think that you will be referring several times in the course of this paper to hemolytic potency and cytolytic potency as well. It might be good for us if you were to tell us exactly what that consists of.

I understand those are more or less classic tests which are carried out, but perhaps for the record you might explain first, what is hemolytic potency? What does it consist of and why do you say there is a relation between it and the concentration of magnesium for various fibers?

A. Well, without going into the fine details of the recipe how you carry the test, hemolytic potency is, as you have said, an in vitro test. It uses...could I use the board... it uses ...this in vitro test is a test in which you are using red blood cells, abbreviated - RBC - you can see that in various papers, RBC is red blood cells.

Now, one is taking suspension of red blood cells... suspension is not the solution...you have a given number of red

A. (cont'd.) blood cells, and whenever these blood cells are in a liquid...of course they have to be in a liquid environment, a liquid milieu...if I magnify one red blood cell, this would be one red blood cell, human red blood cell, it does not have a nucleus. Some red blood cells of other animal species do contain a nucleus, but the human red blood cell, that red blood cell, does not contain a nucleus.

What it does contain is protein, which we all know as hemoglobin. Now normally this hemoglobin is enclosed in a cell membrane, and normally the hemoglobin is held within the boundaries of that membrane.

Whenever situations arise which will modify, chemically modify that membrane, or will rupture, literally rupture that cell membrane, that rupture or that change in the properties of the cell membrane, whenever that happens this is called lysis.

So in general we are talking about cytolysis when we are talking about this rupture or otherwise modification of the cell membrane, which leads to a leakage in the milieu of the contents of the red blood cell. In that particular case, in the case which is particular to the red blood cell, you call this phenomenon hemolysis.

Q. If I may try to simplify it in my own terms, it would mean the ability to, in effect, cause the loss of hemoglobin? That would be hemolysis?

A. That's right. Now, this is the test. What you actually do is you introduce various substances and you study, you measure the extent of this leakage of hemoglobin into the milieu, and you will say substance A is not hemolytic - it doesn't appear to affect the cell membrane and cause the leakage of hemoglobin.

Another substance might do it and you grade this in terms of percentage, percentage being one hundred percent

A. (cont'd.) hemolysis which you produce by very vigorous rupturing of this. This would be the control.

There would be two controls in a usual test - one without any hemolysis at all, and one in which you produce the maximum possible hemolysis. This would be one hundred percent. Then you grade your test samples.

Sample A would be, say eighty percent, of a total possibility of hemolysis.

DR. UFFEN: Is it a volume measurement or a mass?

THE WITNESS: It is the colorimetric measurement, because this is very easily measured colorimetrically. You have a given number, a very precise number of red blood cells which possibly could produce that given amount of hemoglobin, and this is set at one hundred percent for the total hemolysis. Then you grade your substances according to that...some substances, whether they are fibrous materials or dust particles or what have you, gasses, whatever.

So this is what is meant by hemolysis.

Q. While you are on the subject, if you talk about cytolytic, it is the lysis of cyto I would presume, therefore the destruction of a cell?

A. The cytolysis would eventually be the destruction of a cell, but the actual phenomenon is if you take another test of biological material, if you are going to use instead of red blood cells, if you are going to use for instance the macrophage cell, that would be yet another way to measure the effect of some substances on the lysis of the membrane of that particular cell, with ensuing leakage of the cell content into the milieu.

Now, in the case of macrophage, which is quite a different cell, what you would measure as a leakage or as an expression of the damage done to the cell membrane is what leaks

A. (cont'd.) out into the milieu, and what leaks out into the milieu here...in that case it was hemoglobin, in the case of the red blood cell...in that case it would be whatever substances or groups of substances which are contained within the macrophage.

For instance, we know that the macrophage contains enzymes which are quite a good marker of that particular type of cell, and you do essentially the same...it's the same avenue of planning your protocol. You are going to measure the extent to which those enzymes which are representative of the contents of that macrophage - have they or have they not leaked out into the milieu containing these cells.

The same thing here - the extent to which hemoglobin had leaked out into the milieu in which the red blood cells are. Okay?

Now, if we turn to this, if we read again, Allison and Harington - Allison is in the U.K. and Harington is in South Africa - they found a correlation between on the one hand the hemolytic power, as I have explained here, and also the cytolytic potential using macrophage on the one hand. The correlation was made with this and one of the chemical characteristics of chrysotile fiber, namely magnesium which is contained on those fibers.

Q. Dr. Dunnigan, keep in mind that if you want your words to remain for posterity you have to speak into that little instrument there.

A. Ah, oui.

Q. Otherwise you will not remain for posterity.

A. Further evidence that magnesium, according to Allison and Harington, magnesium on the surface of asbestos fiber plays an important role in their action with the membrane comes from studies of the effects of compounds which have the

A. (cont'd.) ability to combine more or less electively with some chemical groups which are on the fiber.

Now, among these chemical compounds you can use are compounds which are called chelating agents. This is the word used by chemists.

These chelating agents have the ability to...how do you say it...so to speak, to grasp or mask or occupy, if you want, very selective atoms, and you have a whole series of...you have a choice, you have a panoply of chelating agents, and if you want to have a chelating agent which will, on the fiber, take care, so to speak of the magnesium ion, you can do this.

Q. Would phosphate be one of them?

A. I will come to that.

Now, what they have done...this is Allison... selected magnesium chelating agents have been claimed to markedly suppress chrysotile hemolysis. Therefore, meaning that you can alter, actually, by one way or another, the chemistry of a fiber and this alteration would lead to a passivation of its biological effect

In other words, it is no longer hemolytic, for instance, in those particular tests.

I thought you had a question, I'm sorry.

Now, these and other data have led Harington to state, and I quote, "These results"...in his mind..."These results leave little room for doubt that the magnesium groups on the surface of the fibers are mainly responsible for the interaction with cell membranes".

Now, the attention has also been drawn on other surface characteristics of the fibers, not only magnesium atoms on the chrysotile fiber.

In 1971, Harington stated that, "Hemolytic activity is not directly related to surface area"...

A. (cont'd.) surface area meaning that you can have a large bundle of individual fibers, or these could be fragmented into individual fibers. In that case here, in that second case here, you would have, of course, a larger surface area than in that case here.

So Harington said that it is not directly related to the surface area.

More recently - and that was in 1977 - Morgan and his associates stated that, "Hemolytic activity was primarily related to specific surface area, and not to the magnesium content of the fibers".

So you see there, almost we can say at the present time there is some discussion as to which of the chemical characteristics is predominant in producing this biological activity.

But overall we can say that even if they disagree on which one, they all agree that surface chemistry is important. The discussion now is which one, which surface characteristic is the important one.

Still more recently, Leight and Wei reported that different forms of asbestos can be activated biologically speaking, or inactivated, by surface charge...not surface area, but surface charge alterations...and they have suggested that the hemolytic activity of asbestos is principally determined by the absolute magnitude of the surface charges that the fiber acquires in solution.

While it is still debated whether chemical or physical properties of chrysotile are responsible for the biological effect, many recent observations have been associated with the chemical surface, the chemistry of the fiber, and their effect on plasmal membrane integrity.

In a very recent paper which was published in 1979, in the British Journal of Industrial Medicine - the paper was entitled, Inhibition by Phospholipids of Hemolytic Action of Asbestos -

A. (cont'd.) the paper is by Jaurand, Magne and Bignon. Professor Jean Bignon is the chief of a very important laboratory in the (French) of Paris, France. He is the head of (Title of laboratory in French).

In that paper they have observed that phospholipids can inhibit the hemolytic action of chrysotile, and furthermore that erythrocytes, this is another word for red blood cell - erythrocyte, erythrocyte hemolysis is a selfinhibiting process.

Q. Perhaps, Dr. Dunnigan, you referred to a paper here...

DR. UFFEN: Could I interrupt just for a minute?

THE WITNESS: Yes.

DR. UFFEN: There is a little step that I really didn't grasp, if it isn't too much a diversion, and that is the relationship between the hemolysis, the destruction of the cell, and cancer-tumors-asbestos.

Just let me know why this is a significant intermediate step.

THE WITNESS: I should have guessed that this very pertinent question was coming along and I would have brought a number of references which state that these hemolytic and macrophage cytotoxicity testings have good correlation with the fibrogenic and carcinogenic potential of the fiber.

I can only...what I could do, I could send you a list of references which are pointing precisely to that point, and one of them would be Lipkin in the U.S.A. He works in one of the institutions...I believe it's NIOSH...of their research, Triangle Park, and if I can quote from memory Lipkin says, "Without any exception, in all cases where we see hemolytic and"...they have to be combined..."and cytoxic effect on macrophage, there is a correlation with the fibrogenic potential and the cancerogenic potential".

DR. UFFEN: My purpose is...you have already answered ninety percent of what I wanted to know...but you pointed out that it's a correlation.

THE WITNESS: That's correct.

DR. UFFEN: Is there also a theoretical or more than one theoretical reason why there should be - without explaining the theory right at the moment?

THE WITNESS: I don't have firsthand experience on that. But I could see that what happens when one's cells are damaged...when they are damaged to the point where the organism must make extra effort to replenish or to reconstruct those cell populations which have destroyed, and it might come to a point where these repair mechanisms, so to speak, could be overhwhelmed, could be exacerbated to the point where in the process of cell multiplication you might have an induction of a wrong transcription, and this might lead into...so this is purely hypothetical, but it is, I think a plausible explanation of that correlation.

Up until this time, that ninety percent of the answer that I gave you is, as you said, a correlation of the observed effect on in vitro systems with the longer-term effectis which might be observed, such as fibrogenicity and cancerogenicity.

This is the reason why these tests have...they are much more rapid, they are obviously cheaper because it takes less time to have data on these tests...I would agree with the statement which would say they are not sufficient tests. If they are used in a screening procedure and within, say a number, one hundred or one thousand compounds, which show these effects, then it would be worthwhile to go further and carry out in vivo testing, which is much more costly and takes a number of months and years to conduct.

M. CASGRAIN: Q. Dr. Dunnigan, in this statement of Jaurand et al, it is stated and I see it in your paper that

Q. (cont'd.) phospholipids are inhibit the hemolytic action of chrysotile. Should I understand by that that when you use the word inhibit that it means that phospholipids, in effect, if they coat the chrysotile will in effect render it passive? Is that correct?

THE WITNESS: A. This is precisely what this paper by Jaurand, Magne and Bignon says.

Q. All right.

A. I can read, if you want, just the abstract that goes as follows, and I quote:

"Hemolysis by asbestos fibers"...and in this case they had used chrysotile..."results from an increase in membrane permeability, and not from rupture of red blood cells".

I repeat this: "And not from rupture of red blood cells.

The effect of chrysotile asbestos on the red blood cells is at least partly, if not completely, attributable to lipid extraction and adsorption onto the fiber."

Q. You say adsorption as opposed to absorption?

A. That's right.

Q. A D S?

A. That is right.

What is meant by lipid extraction, and I mentioned in that paper that these authors said that the hemolysis is a self-inhibiting process. It means that what they have observed when they put, so to speak, in a first step they would use, let's say native...let's call it this way...or untreated, unaltered chrysotile fibers, and these fibers would be in contact with some red blood cells. The contact of these fibers with the red blood cells would cause an alteration by chemical binding here and that, if

A. (cont'd.) we can envisage a stage two type of situation, that particular fiber which has come into contact with the cell membrane would be coated with the lipids which are molecular constituents of a membrane.

Q. If you are going to add...Dr. Dunnigan...if you are going to add papers to this presentation, it has to be identified. Is that...you are giving us the photostatic copies of an extract of that article by Jaurand et al, is that it?

A. No, no. This was taken from a textbook of biochemistry by Linninger.

Q. So you...

A. I used this to explain how the...

Q. Dr. Dunnigan, just to give us a chance, because we must have a chance to put these in order, you have now handed us an extract...how would you describe that extract and we'll put it in as tab ten?

A. A model of cell membrane.

Q. A model of cell membrane which you are producing is tab ten.

EXHIBIT # 40, tab ten: The abovementioned document was then produced and marked.

Q. Now that we have it before us, could you go on with your explanation?

A. Tab ten, you said?

Q. Yes.

A. Okay.

Now, I have photocopied this just to show the molecular arrangement of a cell membrane, and I want to draw your attention to really the lower part, which is a model. You have those little spheres and they are crowding each other like that. This is what you see, okay?

A. (cont'd.) Here and there you have things like that.

Now, I'm not going to draw the whole thing, but this would be the thickness of the cell membrane, okay? And that cell membrane is molecularly arranged in such a way that you have a bilipid layer - that's one lipid here, and that is another lipid here. This is the bilayer of the cell membrane, and every here and there you have a protein molecule. So this would be the inside of the cell - that's the inside of the cell and this would be the exterior.

On those proteins which are on the exterior side, you have carbohydrate groupings, and not on the inside. So what in essence Bignon, Jaurand and Magne said is that when the fiber is in contact with part of the cell membrane, it extracts some phospholipids, part of the molecular arrangement of that cell membrane, and this would lead into a..not essentially a rupture as if you were to rip a garment or what have you...it doesn't have to be so. It may be just one part of the membrane that is ripped away. This would alter the dynamics of exchanges through the cell membrane in such a way that this would be called the damage to the cell membrane, which would lead to leakage of the cell constituents.

Now, what Bignon, Jaurand and Magne have said is that when these fibers come in contact with the cell membrane, they extract phospholipids, and therefore they said, if that particular fiber was resubmitted in a second vial containing red blood cells, part of that fiber is already saturated with phospholipids and it comes to a point, if you take step three, you retrieve these fibers and put them in a third batch of brand new red blood cells, they are not active any more because their active groups on the surface have been saturated and there is no biological effect.

A. (cont'd.) So, here again you have this accent on the chemistry, not on the geometry. You don't have to have a rupture or this view of little, nasty needles piercing through walls. It is not...well, the current...what I call the current, but the late research results that are coming out now, the accent is on the chemistry of it, of the fiber.

Q. Dr. Dunnigan, we have heard evidence here that macrophages play an important part in the defence mechanism of the lung inasmuch as they are able to coat the fiber and eventually permit it to be expelled through the usual mechanism.

You have now spoken about phospholipids. Should I understand that in addition to the effect of macrophages you have the effect of the phospholipids, which indeed inhibit the hemolytic action of chrysotile fiber and that therefore you have those two combined to help the lung defend itself? Would that be a proper statement to make?

I see Mr. Laskin's head moving the wrong way.

A. Oui. I follow your eyes and he happens to be in line with the microphone.

Q. It's because he was using the microphone.

A. Yes, indeed. I would think that this would not be the second mechanism of protection. It would be one of the naturally-occurring phenomenon of passivating the biological aggressivity of any number of constituents. Mind you, these phospholipids which may come from the actual ripping of cell constituents, but they could also come, I would think - although I am not a lung pathologist - but I would be tempted to think that a good part of it could come from a secretion, a normal physiological secretion of some of the cells which are found in the lung. That secretion is called the surfactant. It is secreted by one of the pneumocytes whose function it is to elaborate a secretion which is called a surfactant, and in that

A. (cont'd.) particular secretion you have a tremendous concentration of phospholipids.

So this is one of the many possible mechanisms that the lung has to coat or otherwise attenuate, if not completely annihilate, lung aggressants, whether they be fibrous particles, whether they be anything you might think of which can be coated with, among other things, phospholipids.

Q. When you talk about the effects of phospholipids on the fiber, and the macrophages would be the same thing, I presume, you are talking about chrysotile. Do you know of any similar work having to do with crocodilite or amosite?

A. No, sir.

Q. Do you know any other experiments carried out with chrysotile?

A. Chrysotile? By Bignon. This is right.

There may be, but to my knowledge...

Q. Do you know from material you may have read or from experience, whether there is sort of a...what is the limit at which the defence mechanism, if I may call it that way, involving phospholipids, do you know when that would be accomplished? You have no way of telling us that, do you?

Is there a threshold where this effect is no longer...?

A. As I said, this phenomenon takes place normally. It's a physiological thing to have chemical compounds of the surfactant, which I have mentioned.

Q. It happens to every fiber that comes into the...?

A. Well, I haven't watched every single one, but what I say is that this is one of the many physiological mechanisms by which particles, foreign particles - whether they be pollens or whether they be organic fibers or what have you, or mineral

A. (cont'd.) fibers or dusts or anything which has reached that point - to be coated.

But there again, if I may use the expression which I have used earlier, I suppose there would come a limit where these physiological phenomena cannot cope with, and they are overwhelmed.

There is an additional consideration. That particular point is very different from one individual to another. There is the question of individual susceptibility.

In other words, some people can cope with, so to speak, larger aggressions of the environment, whereas others cannot cope with it. It could come to the limit where...I suppose you have all seen in the papers and on TV these pathetic scenes of children which genetically have not these protective mechanisms which the normal population have. You see these children who have to live their whole life through in some sort of a bubble or tent because they have not...and everything that has to go inside must be filtered and what have you.

Well, thank God we have those protective mechanisms because I wouldn't like the idea of spending my life under a tent like this.

So I don't know if this answers your question, but there are not only two, but many, many protection mechanisms.

Q. Could you go on?

A. Well, I would like to, yes, go on with this hypothesis which I have referred to. This chemical hypothesis is really what set our group on studying the possibility that one could alter the chemical surface of the fibers in the hope that in turn these alterations could have an impact on their biological activity.

There are a limited number of efforts which have been done, and I have given an example of this - Dr. Paul Pezzoli, who is working for Dow Chemical, has tried to chemically

A. (cont'd.) modify the surface of chrysotile fibers with various metal tungstate, and indeed he has succeeded in keeping the useful properties, technological properties of the fibers, and at the same time reducing the biological potency of the fibers.

So this is one example. And we in Sherbrooke were working at this, and during the course of our studies we came across a publication - I don't know if we are going to tab this, but...

Q. If you are going to refer to it, you'll have to tab it. But that's all right.

A. If I could give you...because I have only one copy...but what I wanted to show is...I have a slide from that publication.

Maybe I will give this publication here.

Okay, during the course of our studies we came across a publication by Langer, L A N G E R, Wolff, W O L F F, Rohl, R O H L, and Selikoff. This was published in 1978 in the Journal of Toxicology and Environmental Health, Volume Four, page 173 to 188.

A. Before you go on...

M. CASGRAIN: We will tab this as tab ten...tab eleven, I'm sorry.

EXHIBIT # 40, TAB 11: The abovementioned document was then produced and marked.

THE WITNESS: A. The title of this publication is, Variation of Properties of Chrysotile Asbestos Subjected to Milling.

I have prepared one slide from their publication to show you, I think we will have to...

M. CASGRAIN: Turn off the lights, perhaps?

THE WITNESS: Turn off the lights, and I see

THE WITNESS: (cont'd.) this morning that this...

M. CASGRAIN: Perhaps you don't need to turn off the light. It seems to be okay.

THE WITNESS: I will read from their abstract:

"Mechanical milling is commonly used to produce short chrysotile asbestos for experimental purposes. Such manipulations also decrease fiber crystallinity, alter SiO and MgO interlayer bonding and decreases hemolytic potency and antagonist sorption capabilities.

The degree of alteration is related to the time of milling. Results of biological experimentation with these materials must be interpreted with caution".

Now, if I turn to this, the reason why experimental biologists want to have short fibers is because they want to have fibers which are appropriate for their in vitro testing.

There are various ways to have very short fibers which would be appropriate, and one of them - which was used - is ball milling. For some time people arrived at the conclusion that very short fibers are not, in their words, biologically interesting because well, the shorter you get with ball milling, the lesser you have a biological effect.

This is shown on the lower part where you have cylinder milling time in seconds. So you see that you could obtain with untreated fibers eighty percent of hemolysis produced in one given set of experiments.

Whereas, if you were to obtain shorter fibers by milling for three thousand, six hundred seconds, you are losing your biological activity as expressed by hemolysis. It goes from eighty to twelve.

A. (cont'd.) What these people, who are from the Mount Sinai...well you know, of course, the name Selikoff...have found is that if you are going to take an infrared spectrum of those fibers, what you begin to see is that with ball milling you have a chemical alteration which is expressed by the almost - not quite here - but almost disappearance of the peak of absorption at 1020.

You have, in other words, these three peaks that you see here are very characteristic of chrysotile fibers. That peak happened at 1080 as a wave number, the second peak at 1020, and the third peak at 1055 - that's an error here - at 925, it should read 955, okay? You will see it in the paper.

What happens with ball milling, in order to do short fibers, which will reduce the biological activity, that mid-peak seems to be disappearing.

DR. UFFEN: Is there any difference between ball milling and cylinder milling, or are they synonymous?

THE WITNESS: It is synonymous, sir. It is synonymous.

So these people have found that there is some relationship with biological activity and one, at least one, chemical parameter - namely the intensity of absorption of the infrared spectrum at 1020.

And their conclusion, which I will read from page 185 in that paper, is as follows: It's the fourth line on page 185:

"In studies using short fibers obtained by less vigorous methods"...namely not ball milling, mechanical grinding..."such as air-elutriation or water fractionation,"...which are less vigorous methods... "significant responses in animals were observed. In studies where fibers were reduced in size by vigorous mechanical methods, either no or

THE WITNESS: (cont'd.) "significantly reduced responses were observed."

So in my view these people are relating one parameter of biological activity - namely, hemolysis - to one chemical parameter, which is the infrared spectrum at that particular wavelength.

Now, here is another that's just...this was published last year, 1980, by Dr. Spurny, who shows that again ball milling for the obtaining of short chrysotile fiber will change the chemistry of the fiber, and if it does that, Spurny says, and I quote his conclusion:

> "The results of our very restricted measurements have shown that long-term milling procedures change not only the size distribution, but also the shape and crystal structure of asbestos fibers. They are not, therefore, recommended as comminution methods for preparation of fibrous material used in biological experiments".

I would like to remind you that the first, the most important man who said that biological activity is related, whether you look at it any way, shape or form, it is related to geometry - Dr. Merv Stanton. This is so famous that it has come to be known as the Stanton Hypothesis.

Dr. Stanton used precisely ball milling to produce his short fibers, and therefore we are now, by using physical/chemical parameters such as x-ray diffraction data, or infrared spection data, and we should, I think, use all parameters possible to find out what happens when we are producing fibers for biological experimentation.

Maybe the geometry is not the whole thing. It is

A. (cont'd.) very highly possible that the chemistry is possible, as we have seen in that first slide.

DR. DUPRE: Just before you take that off, Dr. Dunnigan, what do the axes measure on the graph? The vertical and the horizontal.

THE WITNESS: Oh, this is the absorption, just the absorption of x-ray diffraction and absorption...so I could deposit this paper, the Spurny paper...

M. CASGRAIN: It would be tab twelve.

THE WITNESS: It would be tab twelve? Well, then I would have to give the full...or could I just put it here?

EXHIBIT # 40, TAB 12: The abovementioned document was then produced and marked.

THE WITNESS: The only hesitation I have is that these are my only copies. Could I have a copy of this?

M. CASGRAIN: Oh, you can trust Miss Kahn. She does give back copies.

THE WITNESS: Okay.

This is the results of experiments we carried...there we are...this is an infrared spectrum...well, these are four infrared spectra of the uppermost chrysotile fibers. This is the full spectrum.

You will remember that when I showed data from Langer and Selikoff and so on, I took only that part which was pertinent to my discussion - namely, these three characteristic absorption peaks.

Now, if you treat chrysotile fibers with a solution of sodium phosphate, for instance, you realize that you still have your three peaks, and unpublished data to this date, but they will be published at the patent, show that as long as you have these three characterizing peaks, you still have biological activity.

Q. When you talk phosphate, was that the formula that appears on the second line? What is it called?

A. Sodium phosphate - NaH_2PO_4. This is one possibility to treat fibers with phosphate.

Now we have devised another way to...

Q. Before you go on, Dr. Dunnigan, is it correct to state that in the past attempts had been made to treat the fibers with phosphate?

A. Yes.

Q. Although not with the same result as you are about to talk to us about?

A. That's right.

Q. When you talk about the sodium...

A. These examples that we have seen in the past, here's one right there - the treatment with NaH_2PO_4 - sodium phosphate.

Now, we have devised a patented process which uses $POCL_3$ - oxychloride phosphate - $POCL_3$. Now, that treatment is given in the form of a gas treatment. It's gas vapors.

Now, this particular treatment results in the total disappearance of that particular peak at 1020, which you will recall in Drs. Langer's and Selikoff's paper was related to a passivation of one of the biological effects, which is hemolysis.

So here again is an example...oh, by the way...I haven't said it, but from now on I'm going to say it...this is coincident with a passivation of biological effect. That treatment resulting in the disappearance of one of the three characterising peaks in the infrared spectrum - namely at 1020 - is coincident with the passivation of biological effects as was shown in 1978 by the paper by Langer.

So...well, I wouldn't like to take too long a time with this particular paper, because the object of my presentation

A. (cont'd.) is...we haven't got to it yet. But it is that hypothesis which has inspired our group to try to see if chemical alterations, and which one, could result in biological passivation.

Now, if this were so, that the observed biological effects are due to at least partially, if not totally, the chemistry of the fibers, then we should look into what happens in the technological fillyair (PH F.) in which one is using chrysotile fibers, mixes them with a number of chemicals - whether it's cement, whether it's resins, polyolefins, or what have you, and see what is the chemical modification and if these chemical modifications have not modified or altered the biological effects.

It's in that sense that I have prepared this document which are some thoughts which were inspired by this sort of a long introduction of this morning.

M. CASGRAIN: I was going to suggest that perhaps we should interrupt here, for the time being, and if you have any questions...?

DR. MUSTARD: I have one question I would like to ask at this moment.

Could you give me what criteria you used to ensure that when you are doing all this modification that the fiber's physical size and dimensions remains unchanged? We've been through a long theory, we've talked about that, so I guess I would like to know - is this controlled by electron microscopy surveillance? And if so, how is it objectively monitored?

THE WITNESS: Yes. In other words, when these effects are observed, the test materials, whether it's untreated chrysotile or sodium phosphate treated chrysotile, or $POCL_3$ treated chrysotile, or what have you, whatever treatment it is, we make sure that not only so many micrograms of chrysotile, treated or untreated fibers, are submitted to the experimental design, but

A. (cont'd.) also the distribution and the actual examination under electron microscopy.

So in other words, what we are comparing is only... we feel that what we are comparing is only the chemistry of it and not the shape or something else...or the length distribution, if you will.

DR. MUSTARD: What I would require to be satisfied that this is not an alternative explanation, is actual distribution curve of particle size and all the dimensions which are considered to be important - length and diameter.

THE WITNESS: Yes.

DR. MUSTARD: Having heard one expert witness talk about the complexity of that and the time that is involved in doing that, I wonder if this is being done in the kind of detail that will satisfy a critic like myself who would want to pose the other hypothesis. Do you actually have the distribution data or particle sizes both in terms of length and diameter?

THE WITNESS: That's right. That is right, sir.

DR. MUSTARD: How is that determined? Who does that?

THE WITNESS: It's by electron microscopy at the University of Sherbrooke, by Professors Frank Kimberley and Denis Nadeau.

DR. MUSTARD: All the samples he would receive are uncoded? In other words, he has to do the assessment to find out what the treatment is?

THE WITNESS: Yes, that is right.

DR. MUSTARD: Thank you.

THE WITNESS: I must add that...I think it's useful to add that these samples have been sent blindly described - you know, A, B, C, D, E, F, G - to a number of research people in Canada, and in the U.K., in Cardiff, and now that the patented procedure has been completed and the patent has been bought, the company who

THE WITNESS: (cont'd.) has bought the process is planning to send samples all over the world to have this thorough examination.

But my purpose in bringing this up this morning was only to insist on the fact that chemistry of the fiber is at least just as important, because when you try to change the chemistry, this results if passivation of biological effect - as Langer and Selikoff's laboratory have shown in 1978.

M. CASGRAIN: Dr. Dunnigan...

DR. MUSTARD: But do you actually have plots for the distribution curves, that could be seen?

THE WITNESS: Yes, but I don't have them here.

M. CASGRAIN: Q. Could you make them available, Dr. Dunnigan?

THE WITNESS: A. Yes. I could ask Dr. Kimberly to show them.

Q. To make them available?

A. Yes.

Q. Could they be produced as part of your exhibit forty, as say tab thirteen?

A. I'll have to make sure that...well, I will send these to whoever is secretary, I suppose, and he or she will assign the tab number of exhibit number.

Q. Well, it will be tab thirteen and you will undertake to produce them and I will be your intermediary with Miss Kahn, Dr. Dunnigan.

DR. DUPRE: Dr. Uffen?

DR. UFFEN: I have a somewhat similar question, but I'm not referring to size. I am referring now to the temperature. Will you be describing to us, or would you be able to give us, those measures that were invoked to control the temperature while you were doing the $POCL_3$ treatment? Because in your paper that we've had for some time, tab nine, the effects of

DR. UFFEN: (cont'd.) heat treatment were comparable to the effects of $POCL_3$ treatment.

THE WITNESS: That is right. But then what happens is that in efforts like this you have to consider one point. It is not sufficient to biologically passivate fibrous material. They have to be also useful, technologically useful.

What happens is that the heat treatment will not make these fibers very useful.

DR. UFFEN: I don't mean that. I'll put it in a blunt way: How do you know it was the $POCL_3$ that produced the results and not the temperature of the...

THE WITNESS: Oh. Because we have separate groups - one $POCL_3$ treated without heat treatment. Oh, yes, of course.

DR. UFFEN: Well, we would need that also.

M. CASGRAIN: Q. Could you also produce that data?

THE WITNESS: A. Well, I have given you the information that they should be made public when the patenting processes are completed. I know that...how would you say...this is completed, but then it has to be translated into I don't know how many languages and so on.

M. CASGRAIN: I think what Dr. Dunnigan is trying to say is that what you are addressing yourself now is really the inside patent itself and it has yet to be...

THE WITNESS: Released, yes.

DR. UFFEN: It's very crucial, I would think.

M. CASGRAIN: It is. It's been tried several times to...

THE WITNESS: It would be, if I may say so, it would be crucial for that particular discussion that we had, but I repeat, this was to...this was not my...how can I say that...the actual message that I wanted to carry was that geometry, in the view of a number of people, is not the only link. Chemistry is, and

THE WITNESS: (cont'd.) therefore when people are measuring, for instance, what they observe under the microscope as being a fiber, what kind of a fiber is this, optically it might look like virgin fiber - but chemically what is it? Is it chemically altered, and if so, in what way?

Mind you, theoretically it could be chemically altered in such a way that it could be more biologically active or less biologically active, but that's the only message that I want to give to this Commission.

DR. UFFEN: Perhaps I might put a question now which is tied into this whole question.

What happens if you do the red cell hemolysis test using glass fibers?

THE WITNESS: If I could recall...I don't think I could recall what are the effects of glass fibers, but I can say that some components of glass, namely quartz, dust, or silica dust, are hemolytic and cytotoxic.

DR. MUSTARD: That's correct, and the reason for my question is that it's well understood that red cells will hemolyze because of mechanical effects of shearing. It's a well-known biological anomaly.

One of the problems I have with the assay system, that I put forward here, is if the red cells are being diluted up in a medium which is not physiological. It's simply a Veronal buffer, there is not even any sodium chloride in it.

THE WITNESS: That's right.

DR. MUSTARD: Those red cells are therefore in an extremely stressed state biologically in terms of maintaining the normal membrane function. Therefore, when you expose those red cells to mechanical interaction with fibers, and the fibers can be biologically fibers such as you produce when you touch blood on fiber, you can if you force the cells to interact with those,

DR. MUSTARD: (cont'd.) they will shear on you and hemolyze. So I'm trying to sort out in terms of this assay that is being used in the evidence that is being presented, how much of it is related to a theory that you put forward which has some attraction, and how much of it is related to the well-known mechanical effects that will cause red cell hemolysis - including hemolysis in simple in vitro test systems.

For example, if you put red cells through glass wool, just let them flow through that, you'll get hemolysis.

THE WITNESS: They will rupture.

DR. MUSTARD: Well, probably its...and if you increase the flow rate you will increase the rate as well, which is part of the shear effect, so that I think for some of us who have a background in the field it's extremely important that we have a clear understanding about the physical property of the fibers as well as the chemical changes, and I don't think we should go into it, but that's the reasoning for the question and I think Dr. Uffen's question is extremely important and therefore I was extremely intrigued as to why when you heat the fibers they are not very useful commercially, because that suggests there is a change in the properties of the fibers and I would be interested to know whether that is strictly just a chemical change or whether there is also a physical change with that.

Do you know the reason for this? The reason why the heat effect changes the fibers?

THE WITNESS: The mechanical properties of the fibers?

DR. MUSTARD: Yes.

THE WITNESS: Well, you can heat them up to a point where you have a dehydration. Then up to a temperature where you have dehydroxylation. Then there comes a point where you have a total...I'm not a geologist, but that's what I'm told by geologists... there comes a point where there is a total reorgnization of the

THE WITNESS: (cont'd.) crystal structure and this is a new compound totally, and it's called phosphorite.

You have...that compound may have the skeleton of a fibrous structure, but it's extremely brittle. It doesn't seem to have these inner chemical bindings which will make this fiber useful technologically, if it becomes very brittle. This would be phosphorite.

Now, if I may try and add some...I'm not sure I'm going to answer your questions about the shearing effect of fibrous materials on the red blood cells, but isn't that, however, interesting that in Jaurand and Bignon's paper they seem to have succeeded in affecting the surface chemistry of those fibers and then they have no hemolysis.

DR. MUSTARD: I think that's extremely interesting and a crucial question.

There is, of course, the quality of the evidence that there is absolutely no change in the fiber dimensions that are going into the test system. That becomes part of the complexity of the problem, you see.

THE WITNESS: You are right.

DR. MUSTARD: That's the reason for asking for that other evidence.

THE WITNESS: That's right.

M. CASGRAIN: Mr. Chairman, I think that Dr. Dunnigan is about to pass on to the exhibit forty itself, and maybe it's a good time to break, although I would have one question beforehand that struck me from Dr. Mustard's question, and then we can break.

Dr. Dunnigan, when you talk about heating the fiber, when you ash the fiber obviously you heated the fiber as much as you can, or heat the fiber at least when you ash it?

THE WITNESS: A. Well, I would have to understand what you mean by ashing.

Q. When you do electron microscopy, for instance, one type of electron microscopy, where prior to reading you ash the fiber, or the dust shall we say, so that you end up only with the asbestos fiber.

If it is thus ashed, would it change (a) the chemical charactertistics of the fiber and do you know of anything in this connection, and (b) does it change the geometry of it?

A. Well, I think we have to say why this ashing procedure is done. For instance, it might be to when pathologists, I suppose, do obtain biopsies, a lung biopsy, and they want to see if in that piece of lung tissue there are some fibrous material and what it is. So they would have to ash these biological samples and that would be one of the ways to prepare the samples to examine under the electron microscope.

What you would be left with would be possibly altered fibers, but at least they are there and the purpose of doing this is to see were there fibers. They could be intact or it could be their skeleton, if you want, but I think it is...

Q. The skeleton would remain, in other words?

A. That's right.

Q. Okay.

A. The ashing procedure is for doing just that.

DR. UFFEN: The temperature would be enough to do away with the nonsiliceous material, or burn it, is that the idea? Get rid of the...

THE WITNESS: Of the organic, that's right. That's the idea.

DR. UFFEN: Would that be a much lower temperature than the temperature required to alter the siliceous material?

THE WITNESS: I don't know. I don't know exactly what temperature these people are carrying on the ashing process at.

DR. UFFEN: I can get burned at a very low temperature.

THE WITNESS: Yes, sunburn.

M. CASGRAIN: So, Mr. Chairman, perhaps you would like to adjourn now.

DR. DUPRE: Shall we break for about fifteen minutes?

THE INQUIRY RECESSED

- - - - - - - - - - - -

THE INQUIRY RESUMED

DR. DUPRE: M. Casgrain, will you proceed, please?

M. CASGRAIN: Q. Dr. Dunnigan, I think we should now turn to your presentation, being exhibit forty, and as we stated at the outset, this presentation is really dealing with the use of asbestos products in keeping with item four of the mandate of this Commission.

So would you please proceed, and I see that you have about seven pages of material. Perhaps you could leave through it with us and indicate to us which are the sections in the tab we should pay more attention to.

THE WITNESS: A. Yes, sir. As you have said, this is presented to the Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos, and therefore it deals with that particular aspect - the use of asbestos.

Therefore, I mean the finished product, or more generally, end uses of it.

I think the best thing is to read together this presentation.

Most data published to this date on the biological effects of chrysotile asbestos can be divided into two main categories - epidemiological surveys and biological experimentation in animal models, and tissue and cellular systems.

THE WITNESS: (cont'd.) The bulk of epidemiological data are either related to health effects observed in asbestos mining and milling workers after relatively-long exposures of high levels of what I would call native fibers, conditions which have prevailed before low-level standards were implemented in the industry, or these epidemiological data may be related to the health effects observed in workers of specialized trades.

For example - insulation workers using sprayed asbestos in structural steel, or shipbuilding activities, again using native, so to speak, or chemically unchanged fibers.

Data from biological experimentation published in the past have been, for the great majority, based on the facts observed in in vivo and in vitro systems using Union International Contre le Cancer, UICC, samples of asbestos.

Again, the data obtained from these experimentations must be ascribed to effects produced by...I should say presumably chemically unaltered asbestos fibers. That is, native fibers.

As a result, government health protection agencies in many countries, including Canada, have over the years issued laws and regulations governing the use of asbestos. Employers, labour unions, government agencies and the media have all dealt with the problem with varying degrees of intensity and interest. The attitudes range from regulating the handling and use of asbestos by applying the so-called 'best available technology', to the total ban of all forms of asbestos and asbestos-based products.

But all have based their actions on the basis of health effects and biological data arising from exposure to native asbestos. The purpose of this presentation to the Royal Commission on Matters of Health and Safety Arising from the Use of Asbestos in Ontario is to allow the Commission to re-examine the basis of its eventual recommendations in the light of the more recent scientific data which show that a clear distinction must be made

THE WITNESS: (cont'd.) between the biological hazards attributed to raw or native asbestos, and those of chemically unaltered asbestos.

First a word about definitions. It must first be recognized that the word asbestos is not a scientific term. According to the American Geological Institute, the word asbestos is defined as a commercial term, and you will see in tab one that taken from the Glossary of Geology of the American Geological Institute, if you go to the word asbestos it is a commercial term applied to a group of highly-fibrous silicate materials that readily separate into long, thin, strong fibers of sufficient flexibility to be woven, are heat resistant, chemically inert, and possess a high electric insulation and therefore are suitable for uses in yarn, cloth, paper...Hmm, there is an error, of course, here...paint instead of paing, brake linings, tiles, insulation, cement, fillers and filters, and so on and so forth.

The quotation is really from this Glossary of Geology.

It is my opinion that in a scientific study one should always be using the scientific terminology. This is necessary in order that the reader will readily know to which fibrous silicate can be precisely ascribed the reported biological effects. Unfortunately, this is not always the case and the reader may often be misled, even to the point of being brought to compare situations in which the observed biological effects are due to exposure to totally different fibrous silicates.

An example of such a situation can be seen in table fourteen, of a brochure entitled Criteria Document for Swedish Occupational Standards, which was submitted by W.J. Nicholson to the Swedish government in 1981.

M. CASGRAIN: I think this is produced in the record of this particular inquiry, if I'm not mistaken.

THE WITNESS: Yes.

M. CASGRAIN: We might perhaps at this time try and trace the tab number, the exhibit number of it.

MR. HARDY: I believe it's tab ten in the Nicholson collection.

MISS KAHN: It's in the exhibit which is exhibit nineteen.

M. CASGRAIN: Exhibit nineteen, tab...?

MR. LASKIN: It's tab nine.

M. CASGRAIN: Tab nine. All right.

THE WITNESS: Now, this table fourteen which summarizes the results of epidemiological surveys by different authors is presented to show the results of exposure to, and I quote, "asbestos".

The discussion which accompanies this table not only does not help in determining which fiber silicates were involved in each survey, but more seriously leads the reader into making comparisons of results observed after exposure to, quote, "asbestos", and possibly even drawing conclusions on lung cancer risk from such erroneous comparisons.

M. CASGRAIN: Q. Could you show us what you mean by referring to table fourteen?

THE WITNESS: A. Well, in the discussion of this table fourteen there were eight epidemiological surveys and they were all grouped together under the title, Estimated Risk Increases Associated with Asbestos Exposure.

The author says, and I quote from page 55 of that criteria document: "Circumstances unique to a study, statistical aberrations or difficulties in methodology, as previously discussed, may be responsible for this variability.

For example, high values for amosite product manufacturing may arise because of size dependence

A. (cont'd.) "on the biological effects of fiber. In other circumstances, in which chrysotile is used, discrepancies may still remain in comparisons..." and so on and so forth.

And he says: "Because of the wide range of values and the different study circumstances it is not appropriate to average or otherwise combine the data."

But in the last paragraph of that page 55, it is said, and I quote: "What can be said from the data in table fourteen is that the lung cancer risk in three separate studies, by three different groups, is between five and nine percent per fiber year per ML of asbestos exposure".

Which leaves the other eight studies with a much lower percentage. In other words, what I see is that if you were to pick, why pick those particular three studies which show a lung cancer percentage from five point three, to eight point four, to nine point one? One has to realize that in these three studies, two, if you take the trouble to go into the literature and reading the studies, these are, in the first case, amosite exposure, and in the second, it's a combination of amosite, crocidolite and chrysotile.

In the third study, there is no way for us to know because it's in press. If you go in the reference, it's in press.

Therefore it is of the utmost importance to say that when we have an increase in lung cancer in one situation, it must be ascribed not to 'asbestos', which is a commercial term. It must be ascribed to a specific chemical entity which is called either amosite, crocidolite or chrysotile, or what have you.

One would hardly expect to see comparisons made, let alone conclusions drawn, on the effects of exposure to toxic

THE WITNESS: (cont'd.) metal fumes, for instance, without an indication as to which metal is involved. Is it mercury? Is it nickel? Is it chromium, or what have you?

At this point I think it is important to bring in additional considerations. I just mentioned the importance of reporting results of exposure to scientifically-defined material, and I said that no one would expect to see biological data resulting from exposure to toxic metal fumes, for instance, without the exact indication as to which metal is involved.

But I think it is also abundantly clear that such metals are not toxic in all forms in which they might come in contact with humans, or with the environment in general.

The use of chromium, for instance, is a good example which will illustrate this point. Chromium is used in many applications. It is used as an alloy in cars, in surgical instruments and such household items as kitchen utensils.

Clearly, there are uses of this metal which, in the special form in which it is used, do not appear to present a health hazard, while it may still exist in other chemically-defined forms which do present a risk....if these recognized forms are handled without appropriate control.

Let us now turn to one of the commercial varieties of asbestos - chrysotile.

I said earlier that it must be recognized that in the majority of studies related to emission of asbestos fibers, there is an unstated presumption that the fibrous particles emitted from asbestos-based products are intact, and in all aspects - physically, chemically or otherwise - similar to what they were before their incorporation into the composite mixture of the finished product, or end use.

Barring a few exceptions, such a presumption is not supported scientifically, and on that score a recent report

THE WITNESS: (cont'd.) to the United States Protection Agency...the report is EPA 600/1 1979 - 063, July, 1979...states that, and I quote:

> "Further work should be undertaken concerning the physical and chemical properties of asbestos fibers, and the biological effects of altering these properties."

End of quote.

Distinctions between the use of pure, native chrysotile and asbestos-containing finished products have been mentioned occasionally in the past. In a paper which appeared in 1978, and this is tab two..this paper was published in the proceedings of a working conference held at the...in Lyon, France. This paper is by Nicholson and Pundsack.

If you turn to tab two, page 126, at the bottom of the righthand column, the last paragraph starts with, "Once

> an asbestos-containing product has been manufactured whether or not it constitutes a source of asbestos in the environment will depend to a great extent on whether or not the asbestos is firmly locked in the product with a binder, saturant, coating or bonding agent, such that normal handling, application and use do not release it.
>
> Asbestos-cement products are a good example of locked-in products which probably do not constitute a significant source of asbestos to the environment under normal conditions of use".

End of tab two.

However, the difference between the various uses of, quote, "asbestos" does not lie only in the fact that asbestos is less likely to be released from locked-in asbestos materials

THE WITNESS: (cont'd.) than from materials in which asbestos is in the free form.

There is, to my view, a more important additional difference when we consider some asbestos-containing finished products such as asbestos cement, brake linings, molded thermosetting resin objects, etc.

Numerous data can be found in the scientific literature which shows that the incorporation of asbestos fibers into a composite mixture results in the alteration of the physical chemical characteristics of the asbestos fibers.

We will mention only two cases to illustrate the point: Case one will be asbestos in thermosetting resin.

In a publication entitled, Detection of Chrysotile Asbestos in Airborne Dust from Thermosetting Resin Grinding, which was published in 1975 in the Journal of Testing and Evaluation, by Faulring and associates, the authors have found that the number of intact chrysotile fibers emitted varies from one to two per thousand particles, and the authors states, and I quote:

> "Electron microprobe methods are presented that distinguish between chrysotile completely encapsulated in resin and chrysotile with a free surface. The airborne chrysotile in the grinding dust was usually nonfibrous, encapsulated in resin, and closely associated with other materials. In the samples analyzed, the number of chrysotile fibers with a free surface varied from zero to two per thousand dust particles".

If we turn to tab three of this particular article by Faulring, you will see on the first page, 482, the last paragraph of the lefthand column, reads as follows:

"Reference samples prepared from blends of known

THE WITNESS: (cont'd.) "materials and from dust samples produced by grinding chrysotile-bearing thermosetting resins, polyesters, epoxy, were collected by settling in water and on membrane filters in order to obtain the dusts."

Here is how they did it, on the righthand column of that first page, 482. You see sample preparation and description.

So they were using resin plaques containing from zero point eight to eighteen percent chrysotile. These plaques were ground to produce the dusts, with a power-driven hand grinder equipped with a seven inch diameter, sixteen-grit abrasive disc, simulating the fabrication operation found in boatyards and the automobile industry.

At the end of this paragraph it is seen that the edge of these plaques was ground for a period of four to five minutes with a grinder rotating in a direction to throw the heavy particles towards the floor. So they were collecting dusts produced by grinding finished products in terms of chrysotile-containing resins or polyesters, and epoxy, and what have you.

They examined the dust so produced and they came to the conclusion...that would be found on page 489 of the same article by Faulring...the last line of the lefthand column, the very last line of that column on page 489:

"An electron microprobe method was applied to water-collected samples to measure the number of chrysotile particles per thousand dust particles that were either encapsulated in a thin coating of resin, or had a surface exposed to the electron beam. It was found that the chrysotile was usually present as somewhat equidimensional resin encapsulated particles that were frequently conglomerated with other materials. A total of

THE WITNESS: (cont'd.) "two fibrous chrysotile particles was found in four of the studied dust samples, from plaques containing from two to ten percent asbestos."

That conclusion appears, therefore, on the first page of the article, the last paragraph of the abstract.

What this means is that when these people have been forceably producing dust by grinding these finished objects, my way of reading this is that they had to produce at least one thousand dust particles from an asbestos-containing product in order to be able, in some cases, to see a total of two, free fibers.

Now we turn to case two, asbestos and cement.

M. CASGRAIN: Q. I'm sorry, Dr. Dunnigan, if we turn to page 484, do you see an optical microscopy of these fibers? There is a table there on page 484...table two.

THE WITNESS: A. Well, what they did, they were using, as was mentioned, samples in which the dust was settled on water petri dishes and also samples taken by the membrane, filter membrane method. Therefore, this would be the airborne...as it says on table two...the NIOSH method was used, and on the lower part of that table two, in the very center of this lower part, you see Number of Fibers Per Cubic Centimeter of Air.

Do you see that? The lower part of table two, dead center? Number of Fibers Per Cubic Centimeter of Air.

By using the NIOSH filter membrane method, they saw that in sample number one they could not see any fibers. In sample number two, which was ground for four minutes to five minutes and so on, in the method that was described, they could see zero again, and then zero point two, and then one point two, then zero point one, and then one point two, zero zero point nine, and so on.

THE WITNESS: (cont'd.) In other words, you have, in order to produce airborne...in other words, when these finished products are used by the, shall we say the consuming public, you would have to grind these in such a way that you would have to produce one thousand particles in order to see one free fiber, and this, as I read it on table two, would be the equivalent of, in some cases, zero, zero, zero point two, one point two, zero point one and so on, fibers per c.c.

Does that answer your question?

M. CASGRAIN: Q. Yes.

When you talk about thermosetting resin, is this the material which is used for molded plastic objects which encapsulate something?

THE WITNESS: A. That's right.

Q. Where would you see a typical thermosetting resin?

A. I'm not very familiar with the technology...

Q. Casings for motors, perhaps?

A. For instance, like that, in the car industry.

In other words, instead of using straight plastic which would be brittle, they would incorporate fibrous material which would make this finished product less brittle, and they would incorporate up to, as they said, eighteen percent in either resin or polyesters, or what have you, to reinforce it.

Q. Thank you.

A. Now, I would like to turn to case two.

Fairly recent data by Deruyttere, Baeten and Helsen, which incidentally was presented at the same Fourth International Conference in Torino, 1980, as you will see in tab four...show that asbestos fibers undergo important physiochemical modifications resulting from their association with cement, as observed by comparing x-ray fluorescent spectra of virgin fibers...that is, those fibers before they are incorporated...and those of fibers

THE WITNESS: (cont'd.) obtained from cutting or sawing of asbestos-cement sheets and pipes. The authors state, and I quote:

> "Therefore, conclusions which have been reached for pure asbestos dust should not automatically be applied to asbestos-cement dust."

If you turn to tab four, the Deruyttere, Baeten and Helsen publication, I would like you to turn to page 743, which is a figure - figure one and figure two.

What these authors have done is they have used one physiochemical parameter, namely x-ray fluorescence, and they have carried the x-ray fluorescent spectrum on, as they put it, virgin chrysotile fiber, which showed essentially these two characterizing peaks - the first one being magnesium and the second selesium, and in figure two they run the x-ray fluorescent spectrum of, quote, "optically pure", unquote, chrysotile fiber harvested from asbestos-cement dust.

In other words, they have compared a chemical characteristic, namely x-ray fluorescent spectrum, of fibers which optically appear alike. But they observed that those fibers which have been harvested from asbestos-cement test are chemically different inasmuch as x-ray fluorescence spectrum would be one indication of a chemical alteration.

I would also like now to turn to...

DR. UFFEN: Pardon me. You left me a little bit behind there. I may have just misunderstood.

Where did the calcium come from in the spectrum in figure two?

THE WITNESS: I believe we can find it in their own article. Will you please take page 738.

DR. UFFEN: Seven thirty-eight.

THE WITNESS: There is a long paragraph there.

DR. UFFEN: Yes.

THE WITNESS: Let's read the first ten or fifteen lines:

"In figures one to three, an example of the results obtained is given. Figures one and two show x-ray spectrum obtained from a spot analysis of chrysotile fiber respectively in a pure asbestos and in an asbestos-cement sample.

It appears that a spectrum from the optically pure asbestos fiber in the asbestos-cement dust contains a calcium peak not present in the pure asbestos."

Now this is where your question...okay?

DR. UFFEN: Yes.

THE WITNESS: Now, if you read the following sentence:

"This is confirmed by figure three, which shows that the scanning electron and x-ray images of an optically pure asbestos fiber, indicating that the calcium peak in figure two does not originate from some cement particle lying close to the fiber, but that it originates from the whole fiber itself. It can be concluded that the fiber is coated with some calcium-containing compound".

That's the only answer I can give you.

I would like now to draw your attention to the following page, 739. It seems that...and I'm dealing with the adsorption tests.-.it would seem that this chemical modification which has undergone on the chrysotile fiber because of its mixing with asbestos, with cement, would change not only a physical parameter but its ability to be a carrier of so-called carcinogens.

If we can read: "As a preliminary investigation

THE WITNESS: (cont'd.) "of the properties of asbestos-cement dust, the following adsorption experiments have been made. Samples of pure asbestos, pure cement, and asbestos-cement dust have been suspended in solutions of two important carcinogenic agents from tobacco smoke - namely benzopyrine and malic acid hydrazide."

These are recognized carcinogens which are extracted from tobacco smoke.

So what they did is, they made an n-hexane solution of these two carcinogens, and then they made...they put samples of pure asbestos in one case, and of pure cement in another case, and of asbestos-cement dust in another case.

An example of experimental results is given in figure four. In this figure, we shall go to it after that, in this figure the residual concentration of benzopyrine dissolved in n-hexane - this is the solution - after forty hours of contact with dust samples, is drawn versus the initial concentration.

It shows that the adsorption by sheets - NA refers to nonautoclave and A refers to autoclave sheets - the adsorption by these sheets is close to that of hydrated cement dust, and much smaller than the adsorption by pure chrysotile dust.

Let's go and examine this particular figure four.

M. CASGRAIN: Q. It's at page 744, right?

THE WITNESS: A. That's right.

This is n-hexane solution containing the carcinogens, which we will call CA.

In the vial labelled A, you put some virgin chrysotile fiber.

In vial B, you put...they have put cement, pure cement particles.

In vial C, they have put asbestos-cement fibers,

THE WITNESS: (cont'd.) those fibers harvested from the finished products.

What they see is that after forty hours, the potential for adsorption of that carcinogen here, which is all these, if you measure it in terms of what is left in the solution after forty hours, what is left indirectly would be an indication of how much had adsorbed on the fibers, and this is what you see here in this figure four.

You see that the bottom line here is chrysotile, and all the other dust, whether it's hydrated cement or dust harvested from cement, behaved quite differently from the pure chrysotile.

In other words, this means that if pure, native chrysotile could be possibly viewed as a possible carrier of some carcinogen, namely benzopyrine or malic acid or what have you, once that chrysotile has been incorporated into cement, it does not behave any more this way, it behaves this way. And this way is exactly the same way as if it were cement.

In other words, it has lost its ability to carry carcinogens.

Now, I don't know personally to what extent biological or carcinogenic effect attributed to the number of materials is attributed to these particles per se, or to their ability to carry carcinogens from environments. I don't know.

But this view has been expressed, so what can be said here is that there is a vast difference between the chemically unaltered specie and a chemically altered specie, chemically altered in the technological process leading to a finished product.

I see that I have gone a little further than I....

Okay, now let's go now to the middle of page five in my presentation, under the title, Biological Effects

THE WITNESS: (cont'd.) Obtained with Native and Modified Asbestos.

The likelihood that physiochemical modification produced by the very processes of mixing the asbestos fibers with the other compounds of the finished composite result in a modification of the biological effects ascribed to pure or native asbestos has recently been verified, and may be illustrated with two cases.

While I realize that I just mentioned one case, which is on the board - so case one, let's go with case one:

Biological effects of inhaled asbestos-cement dust: In a paper published in 1978 by Wehner and associates, which is tab five, the authors made an inhalation study, and therefore this is an in vivo experimentation, using one hundred and ninety-two hamsters exposed to respirable asbestos aerosols five hours per day, five days per week.

The animals were sacrificed after three, six and fifteen months of exposure. It was found that the asbestos-cement dust whose concentrations were between zero point one and one microgram per liter had no significant effect on body weight and mortality of the animals.

Furthermore, no primary carcinoma of the lung and respiratory tract, and no mesothelioma, were found. By comparison, a one hundred percent incidence of severe asbestosis, and a high incidence of adenomas was observed in hamsters that were exposed to pure chrysotile.

If we go to that...well, top of page six...you will see this in tab five, which is their full paper, and if you turn to page 388 of their paper, the very last paragraph, page 388, it reads as follows:

> "As an alternative explanation for minimal response in hamsters of this study, the hypothesis may be advanced that chemical reactions during mixing of

THE WITNESS: (cont'd.) "the base material, cement powder and asbestos fibers, and their processing into a new material - asbestos cement, change the physiochemical properties of the asbestos fibers and/or possibly coat themwith cement so as to make them less pathogenic.

This hypothesis might appear less attractive in the light of Stanton's finding"...

and so on and so forth.

So clearly, when you read this article the authors make quite a distinction between the results obtained after exposure to pure, chemically unaltered chrysotile and the chrysotile which would be produced and obtained from asbestos-cement finished products.

Now, page six...

DR. MUSTARD: May I ask you a question about that study?

THE WITNESS: Yes.

DR. MUSTARD: Tab five. In my very quick look at the experimental design of the study indicates that in this study the hamsters were only exposed to the asbestos-cement fibers, I think. Is that correct? They did not run a control group of animals exposed to natural asbestos fibers in this actual study?

THE WITNESS: At the same time, you would say?

DR. MUSTARD: That's right.

THE WITNESS: That is right.

DR. MUSTARD: Then they are drawing their conclusion based on experiments by themselves or by other investigators at different time periods, under different conditions?

THE WITNESS: You are quite right, because on top of page 388, the third line, middle of the third line:

"By comparison, a one hundred percent incidence of

THE WITNESS: (cont'd.) "severe asbestosis, high incidence of adenoma was observed in hamsters that were exposed to pure chrysotile".

This was published in 1974 and 1975. So what they did first, they exposed, as you said, to pure chrysotile, and then later they did the same study, using the same species and so on, but it was not coincident in time.

DR. MUSTARD: Therefore we do not know whether the hamsters in Richland, Washington if exposed to natural asbestos fibers would behave as they did in the German study.

THE WITNESS: Oh, they were the same authors.

DR. MUSTARD: But one is done in Germany and one is done in Washington, or am I reading that incorrectly?

It says, "German research"...I see. The studies were done in the same laboratory, is that what you are saying?

THE WITNESS: That's my understanding, sir. Yes. Final report, National Cancer Institute, Pacific Northwest Laboratory, Richland, Washington.

So it's by the same group of people, in the same laboratory, same experimental setup..the difference being that they first produced an experimental model showing very severe asbestosis and so on. Later, they used the same protocol with fibers retrieved from asbestos cement.

Now, we are back on page six, and as I said, I mentioned case two, pure versus asbestos-cement dust as carriers of carcinogenic agents. I will not repeat this because we have seen this on the board. My understanding is that there is some chemical alteration of chrysotile fibers when they come from asbestos cement, which makes them less likely to be carriers of environmental carcinogens.

Well, here's a little personal note. This indicates

THE WITNESS: (cont'd.) that chemical modifications of pure chrysotile fibers altered their ability to act as carriers of known carcinogens. It is noteworthy to mention here that a major environmental cause of lung cancer is inhaled cigarette smoke, which is related to eighty to ninety percent of lung cancer in the U.S.A., as reported recently, and you will find this in tab six. This would be on page 435, in the paragraph under the heading Lung. There is a phrase beginning by: "Other occupationally-related carcinogens for lungs include arsenic, chromium, coal products, iron oxide, mustard gas, nickel, petroleum. But the major environmental cause of lung cancer is inhaled cigarette smoke, which is related to from eighty to ninety percent of lung cancer cases in the U.S.A."

The same view is expressed in the 1979 annual report on the Centre International de Recherche de la Cancer, in Lyon, in the following terms - and you see this in tab seven - and I quote from page twenty of the annual report under the heading Risk Factor, the first one being tobacco, and I quote:

"Most studies in countries where cigarette smoking has been of long duration indicates that from eighty to eighty-five percent of lung cancers are due to cigarettes."

I thought it might be useful to relate this to the observation that fibers which might be emitted from asbestos-cement finished products become less likely to be carriers of these carcinogens.

Well, my personal conclusions of this is that even if we are not, if we might not be absolutely convinced by each individual data which I have been reporting so far, that there is now a sufficiently large body of evidence for me to arrive at

THE WITNESS: (cont'd.) this conclusion, which I will read:

"Regulations concerning the use"...and the key word here is use..."by the consuming public of chemically altered chrysotile in the form of finished products, especially asbestos-cement finished products"...I say this because you may know that somewhere between seventy-five and eighty percent of all chrysotile is used precisely in that form of finished product, asbestos cement.

I'll start again:

"Regulations concerning the use by the consuming public of chemically altered chrysotile in the form of finished products, especially asbestos-cement finished products, based on epidemiological and experimental data obtained with pure or native chrysotile are not supported scientifically. Regulations should therefore discriminate between these end uses of chrysotile in which the fibers have been altered physiochemically and those uses in which pure, chemically unmodified fibers may be emitted.

Dust-sampling data should therefore include the appropriate assessment of physiochemical integrity of the collected fibers, as was recommended recently, in order to be supported scientifically."

I guess that's the main message, Mr. President, I wanted to convey to this Commission.

M. CASGRAIN: Mr. Chairman, I have one question which is not specifically related to that quote, to Dr. Dunnigan and I think it will be a fairly short answer, but it's kind of informative, I think. Perhaps I might put it now?

DR. DUPRE: Please, counsel.

M. CASGRAIN: Q. Dr. Dunnigan, as head of the IRDA, you are aware of the research that is being carried on, and could you perhaps give us a brief summary of the projects which are now underway which would be of interest to this panel, and I might perhaps ask you first to tell us whether in effect any research is being carried on now with respect to the effect of glass fibers?

THE WITNESS: A. Supported by IRDA, you mean?

Q. Yes. As one, and then you might tell us about the others.

If it's going to take...

A. Three minutes?

Q. Okay.

A. The research program, or the funding research program which was set up by IRDA quite recently is involved in two main lines of research, one which would deal with R and D in technology - finding better uses, improved uses of asbestos finished products and therefore that type of research proposals, which are freely submitted by research workers, mostly from academia, would deal with...would not specifically deal with the biological or health issues, and we have a number of research projects, some of which I would not be prepared to disclose at this time because of, again, patent possibilities, but they would involve, you know, innovation, technological innovation.

Other projects, to answer your question, are very much involved in the biological assessment. The biological assessment, in order to differentiate which are the, which would be the proper and safe uses of asbestos in the form of finished products, and admittedly, which would be improper uses of asbestos in the form of a given end use - whether it has been going on in the past, or whether it is being maintained, and so on.

In order to do that, the research which we are

THE WITNESS: (cont'd.) supporting right now and to the tune of what is budgeted for up to the year 1984 in terms of research funding is the sum of two point four million dollars in various individual research projects, and these would include the biological assessment of what we have used, native fibers or fibers which may be modified either experimentally by a given mysterious patented process, or what have you, or modified because of their incorporation in terms of finished products...for instance, asbestos cement...and of other fibers or fibrous material.

Therefore, we are interested in supporting research projects which would involve a quick assessment, that would improve on in vitro biological assay extant, on the significance of these rapid in vitro biological assays, to see if we couldn't find a better, a tighter relationship between the hemolysis and macrophage cytotoxicity and what have you, chemiluminescence and DNA repair mechanisms, and so on, with in vivo systems in which we would have the time to observe what happens in vivo.

In animals, and this might be of interest to you, in animals we are now supporting a project, we are now beginning supporting of a project in which the experimental animal is the sheep. This is being done at the medical school at the University of Sherbrooke, where the sheep will be seeded with various fibrous materials - not only chrysotile, pure chrysotile, but modified chrysotile, calcium carbonate fibers and so on...and possibly some proposed substitutes, glass fibers and so on.

The interesting thing with these animals compared to rats and hamsters, when you are taking a sample from rats and hamsters - that's the end of it, you have lost your animal. But it is possible to follow the installation of pathological processes in an animal like a sheep because it is possible by a technique which is called bronchoalveolar lavage to get samples of the secretions and cells which are in the lung, and at given periods of

THE WITNESS: (cnt'd.) time, and see the evolution in time of single dose or repeated doses and so on.

So this is the type of research...

M. CASGRAIN: Q. What is the life span of a sheep?

THE WITNESS: A. I beg your pardon?

Q. The life span of a sheep is what?

A. I don't know.

Q. It's more than a rat, isn't it?

A. Obviously.

Q. As long as a horse?

A. Possibly. I don't know. I think you would have to ask this to the Welsh who keep sheep, you know, on free rein for years and years in order to collect the wool, and maybe also in Scotland they would give you answers. Here we kill the sheep to get our lamb riblets and so on.

So this is the type of research projects which are examined by scientific committee that IRDA has, whose recommendations are transferred to the governing body of IRDA, and which takes the decision of funding after receiving the recommendations of the scientific committee.

In all, I could tell...I don't know if it's going to take too much time, but yes, I have said it...so far we have commitments for funding of two point four million dollars in both technology and the biology of...

DR. UFFEN: That's for both?

THE WITNESS: Yes, that is for both, but I should say that...

M. CASGRAIN: Q. This is the budget that was voted for this year, is it not?

THE WITNESS: A. When I say two million, it's last year and what we are committed so far, but these projects will take place in, you know, they are thirty-six month research projects and so on. But to answer the question, it is mostly

THE WITNESS: (cont'd.) there where it costs an awful lot of money.

DR. UFFEN: Could you put it in another way? How many people would you have involved, of say two categories, say scientific investigator and support staff? About ten?

THE WITNESS: Professional people? You would say M.D.'s and Ph.D.'s, and chemists and pathologists and immunologists and so on?

DR. UFFEN: Yes.

THE WITNESS: I would count...oh, something like twenty in these individual research projects, but these are assisted with maybe forty technicians, something like that.

DR. UFFEN: Two and a half million dollars over four years? You run a very lean and tight organization.

THE WITNESS: Oh, no...I must tell you, sir...yes, it's very lean and I would like to have more funding.

DR. UFFEN: They must do other things and get paid other monies for...

THE WITNESS: Oh, yes. These would be members of a physiology department, biochemistry department, pathology department, whose salary is paid by the school of medicine or faculty of science and so on. This is the research product, these are more or less the direct costs. We are not so far. I would like to come to that point where we would have people whose salaries are paid for.

M. CASGRAIN: Q. But you mean to say that IRDA is funding research by various groups who come to IRDA?

THE WITNESS: A. That's right. That is right. In exactly the same manner as the Medical Research Council of Canada or the National Research Council of Canada, except that the research projects which we receive are dealing only with asbestos, period. Or fibrous material.

Q. Is there not one research project involving the use of the colon, human tissue and the effect of acid on human tissue when mixed with asbestos fiber?

A. Yes. This is...I am very anxious to see the result of this project because we are aware that there are two heavily-funded studies, one in the U.S.A. and one in France...I know for sure the budget of the U.S. study, which is over a million dollars just for that single study of the effects of ingested asbestos...and when we saw the experimental protocol we thought that the results that would come from the way the protocol is built up would be, well, these are the end results, these are the effects we observed - there is cancer, there is no cancer or to what degree and so on - but they could only say what happened. We would like to know why that thing would happen, and we thought that one of the things that happened when asbestos is ingested, it comes into contact with the extremely acid medium, the stomach contents, which as you know secretes almost one hundred percent pure HCL. The Ph of the acid secretion is something in the neighborhood of one point eight or two, so it's extremely, a violent environment.

So we thought that whatever results might come following the U.S. experimentation, of the French experimentation dealing exactly with this, that we might have an explanation of if there are some or if there are no damaging effects from ingesting asbestos in vast quantities. Nobody would ever dream that we would eat asbestos to that point, but what happened is that these fibers are in contact with first an extremely acidic medium in the stomach, and then down the pathway...this would be the stomach where, as I said, you have almost pure HCL produced there...and then you have the pancreas, and that part of the pancreas which is called the exocrine pancreas, not the endocrine. The endocrine pancreas secretes, amongst other things, insulin.

THE WITNESS: (cont'd.) I'm talking about the exocrine pancreas, that part of the pancreas whose secretions are digestive secretions and which fall into the intestine and so on.

Now, the pancreatic secretions are highly alkaline. We would like to wonder what happens to pure chrysotile, for instance, when it comes first into contact with a highly acidic medium and then, as it follows the GI tract, what happens after that when they are submitted to the highly alkaline secretion of the pancreatic secretions.

So this is one of the projects which is currently being funded by IRDA, so we will wait and see.

M. CASGRAIN: I have no further questions, Mr. Chairman.

DR. DUPRE: Is this, perhaps, a reasonable time to take a luncheon break, it being ten after one? Shall we reconvene at half past two?

THE INQUIRY RECESSED

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THE INQUIRY RESUMED

DR. DUPRE: Do we have an order for cross-examination, counsel?

MR. LASKIN: I'll be short today.

THE WITNESS: Thank you.

MR. LASKIN: I only have a few questions, Dr. Dunnigan.

CROSS-EXAMINATION BY MR. LASKIN

Q. Can I just clear up one point about Dr. Nicholson's criteria document that you referred to in your presentation?

A. Yes.

Q. Looking at table fourteen, the one study that you indicated was in press is, as I understand it, Dr. Dement's... why don't you get the page, page fifty-six.

A. That's right.

Q. Is Dr. Dement's study of the textile plant in the United States.

A. I beg your pardon? I do not understand, I'm sorry.

Q. As I understand it, you referred to the three studies that showed considerable excess risk, and the point you were trying to make, as I understand it, was that Dr. Nicholson did not really set out what kind of asbestos he was talking about.

You then, first of all, referred to the insulation manufacturing study in Paterson, New Jersey, as being amosite?

A. Oui.

Q. That's Dr. Seidman's study. Then you referred to asbestos products manufacturing study in Englan...

A. Newhouse and Berry.

Q. Newhouse and Berry?

A. That's right.

Q. Then the third study, which is the U.S. textile production study as shown in table fourteen..

A. This is right.

Q. ...is, as I understand it, Dr. Dement's chrysotile asbestos study in the United States?

A. This is the title of this communication.

Q. The only question I wanted to understand was, are you suggesting that there was something other than chrysotile that was used in that plant, or are you simply indicating that you had no knowledge at the time that you made your own statement?

A. No. I have no way of knowing if there were other than chrysotile asbestos, but what...the point I was trying to make

A. (cont'd.) is that when you use a table, it's because you have in mind to tabulate, and therefore you want to bring together results of studies which are about asbestos, and I think my message was we should be very clear when we are giving results of...whether it's an epidemiological or a biological study... in always stating what type of scientifically-defined material should be used.

Q. Has your own research gone so far as to suggest to you that there may be different health effects as between the different types of asbestos?

A. Yes, but I must say that we haven't done the full extent of all the fibrous materials, and even of those which are collectively known as asbestos fibers. Some of the observations that we have seen, for instance, is that we are observing possibly the very same thing that other people have observed - for instance that crocidolite tends to be less hemolytic than chrysotile in that particular system.

On the other hand, the cytotoxic potency is different. It's not in the same order. Crocidolite would be cytotoxic.

Q. Just let me understand. Have you, in addition to your experiments with chrysotile, done similar experiments with respect to crocidolite or amosite?

A. Not me, but some of the people who are working...

Q. With you?

A. ...under research grants supported by IRDA. And they are not only doing this, not only chrysotile, crocidolite, but all kinds of fibrous materials, including anthophyllite, erionite, rock wool and all types of fibers which are prepared in collaboration with Dr. Gibbs from McGill University.

So the part of McGill University is to produce the material, characterize it in as much as the characteristics

A. (cont'd.) have been set out in the research contract, which is strictly generating fibrous materials from various ores and having electron microscopy images and then an evaluation of size.

Then these are then assessed with these two assays which I have mentioned this morning.

Q. How far, has that research progressed so far as to enable you to draw any conclusions as to the relative toxicity as between crocidolite on the one hand and chrysotile on the other?

A. The results are now being compiled to be handed over to the agency which has paid for that research, and it is the Quebec Department of Natural Resources.

Yes, that's right, Department de Recherche Naturelle.

This study should be available, I think, within two or three months and the name of the person, if I could give you this much information, is George Dahmen, D A H M E N.

Q. Thank you very much.

DR. DUPRE: This is the name of a contact at the Ministry?

THE WITNESS: That is right.

DR. DUPRE: Mr. Dahmen appeared before us.

MR. LASKIN: Yes, he appeared before us in phase one.

MR. LASKIN: Q. In terms of your own research, would I be putting it fairly if I suggested to you that you are not indicating that we should disregard fiber shape, fiber size in assessing the toxicity of asbestos fibers, but rather that we should not simply look at that alone, but should consider altered chemical properties, chemistry and so on? Is that a fair statement?

THE WITNESS: A. Yes, it is, sir. It is, sir.

In as much as it would seem obvious that fibrous

A. (cont'd.) particles, in order to reach what we could call the target organs or cells, they have to be of a certain size characteristic, of a certain geometry...first of all, to become airborne, second, to become respirable and then to reach that, and in as much as this comes to the obvious conclusion that size considerations are very important.

But I am of the opinion that this is not the complete picture and I tend to be of the opinion that Dr. Harington, that I heard from Dr. Harington, who once said, and it's not very long ago, he said that probably over the years we have been so stricken by the observation by Dr. Stanton's studies on classifying fibers by length and so on, and this seemed to be such a beautiful model that all the research that we did was concerned with associating biological effects with geometry, and all the time we seemed to forget that there could be other things that should be looked at.

What I have given this morning is the relatively newer data which point that one must look also to the chemistry.

Q. Can I ask you in terms of your own research or in terms of what you wrote in tab nine of exhibit forty, have you ever subjected these altered chrysotile fibers to animal experimentation?

A. By this you mean in vivo?

Q. Yes.

A. That's right. I understand your question.

This is now in the process of being done in at least two places - the research contract...because now the patent is sold, it's going to be the owner of this patent who will contract with Dr. Davis' laboratory to study the effects of these modifications in in vivo setup.

As a matter of fact, there is a full research program to further assess the impact of these modifications on biological

A. (cont'd.) systems, whether they are...in other words, not only based these considerations on the only two systems which I showed this morning, which were red blood cell hemolysis and cytotoxicity, which were in vitro, but extending this for the whole range of other in vitro assessments, and in vivo.

Now, the result of the in vivo assessment might take at least about three years to come.

Q. Are you...do we know at this stage, or are you also testing, as to whether the altered fibers have the same useful applications as what you have termed native chrysotile fibers, or is that also a matter that is being tested?

A. Yes, for obvious reasons, the reasons being that you might introduce chemical modification on fibers to the point where they are no longer technologically useful.

Therefore, it's useless. It might be a nice laboratory curiosity, but with no technological advantage.

So it appears from the preliminary data that those fibers which have been phosphated by the gas process are not only biologically passivated, but also technologically very interesting on at least two grounds. But I cannot go further than that without disclosing some of the advantages that the owner of the patent would like to use himself.

Q. Fair enough. But do I take it the message from that is that this research that you are doing is really..it's not at a stage where we are going to see any practical application of it for at least some number of years? It's still in the testing process?

A. The biological assessment testing will go on and on for surely a number of years, but the technological character of that fiber is already being examined very closely with possibly, with a possibility of at least production runs, experimental production runs to be tried in the field maybe within a year or two.

Q. Not to pursue it too much farther, but in terms of its practical application, are you talking about, for example, altering the characteristics of chrysotile during the mining or milling process, or are you talking about some alteration that only will demonstrate itself in an end-use product?

A. No. The alteration would come at the end of the milling process, before the manufacturing process starts.

In other words, they could be treated at the mill before expedition to buyers of cement production...

Q. Textile production...

A. That sort of thing.

Q. Let me just ask you in the midst of this one technical question during the presentation when you referred to the three peaks. Do you recall the slide that was on the board? And said that, as I understood your evidence, when you treated your chrysotile fiber with the process that you, the substance that I take it that now forms the subject of this patent, that one of those peaks disappeared and that was of significance biologically?

A. Yes.

Q. All right. Can you explain that? What is it about the three peaks and what is about the missing peak that affects the biological activity?

A. I really don't know. I think I have to turn to what Mr. Langer, Dr. Langer said about this alteration, and this is exhibit forty, tab eleven, and you will find on page 180... and I want to insist on telling you that I am not a minerologist.

On that page of the test they say?

"A triplet at 1082, 1020 and 955"...one, two, three, four, the fifth line.

Q. Yes.

A. Well, you can say 1080, 1020 and 955, it all depends. It's not that close, all right?

A. (cont'd.) "Possibly corresponding to the Si-O, Si-O-Mg, for the second one, and Si-O(H)-Mg, stretching frequencies as suggested by spectra of quartz, nemalite..." and other types of materials.

So, Dr. Langer relates these absorption peaks to the chemical binding of the constituents of the crystal, and he says that whatever is responsible chemically for that midpeak, for the 1020 peak, whenever that is altered, we see a passivation of biological activity as exemplified by what is seen in table three.

Q. Where does...

A. On page 182.

The more you are going to mill this chrysotile, or the longer you are going to mill the chrysotile, you will have at least a coincidence milling time, disappearance of the peak at 1020, gradual disappearance, and also gradual disappearance of one biological parameter - hemolysis activity.

Q. And also, I take it...

A. So there could be, there must be other ways to look at these chemical changes. Infrared spectrum would be, but I would suppose that there should be far more investigation trying to relate these chemical changes to biological activity.

Q. And use of the fiber, I take it, because one of the things that appears to happen, if my reading of Dr. Langer's article is correct, is that there is a reduced crystallinity in the chrysotile fiber as a result of the application that took place in this article...or is exemplified in this article.

A. As a result of the milling, that's right.

Q. Do you have any information one way or the other as to how that affects the usefulness of the fiber in terms of its strength of anything else?

A. If you are going...my appreciation...I am a

A. (cont'd.) biologist, not an engineer...but my appreciation of this is that if you were to mill these fibers until such time as the midpeak has totally disappeared, you would obtain fibers which are so short that it would be...they wouldn't be useful for some applications. They could be used maybe as fillers, I don't know, but not, certainly not for their structural strength.

Q. I take it when you have gone through these articles with us that you are...I don't want to be unfair to you... but basically doing no more than reporting to us what others have found from the literature...or which you have found from the literature and what others have written about?

A. It is not unfair at all, sir. My idea of reporting here to this Commission was to make this Commission aware that there are other reasons for the ascribed biological effects, and here are some of the more recent reports and this is the only point, really, I wanted to make.

DR. UFFEN: I wouldn't be surprised, however, if the Commissioners wanted to examine you further than that because of your knowledge in the field, and at this point perhaps I could ask a question that is somewhat related.

In your experiments so far have you carried out similar modifications with anything else but the phosphorous? Sodium, potassium or...?

THE WITNESS: No. The main...I have to be careful now because I am not sure if I should, if it would be appropriate in view of the owner, the actual owner of this patent that we should disclose which treatments are successful and which treatments are not successful. But we did repeat some experiments like heating, acid, leaching acid treatment, by strong acid such as HCL, weak acid such as acetic acids, and things like that.

They were mostly wet treatments, wet treatments.

DR. UFFEN: What led you to...do you mind my asking...

MR. LASKIN: No, Dr. Uffen. I think you are about to ask the question that...go ahead.

DR. UFFEN: What led you to use the phosphorous chlorine compound, which you did quite some time ago?

THE WITNESS: Well, this is a team effort, and it came as an observation by one of the members of the team who said that if we are going to try and modify, chemically modify, asbestos fibers, chrysotile, so that we would be able to keep their useful properties, and do this in an economical way, we should avoid water. Because if you are going to treat the result of the dry fibers, as they come out of the mill, put this into an aqueous solution of whatever compound you might wish to treat this fiber with - whether it's sodium phosphate or aluminum phosphate, or what have you - then you would have to remove the water, dry the new, treated fibers and then send it out on the market.

So why don't we look for a treatment which could possibly be active in a different way, in a way which would not involve the removal of water. And that's how we came up with this suggestion - let's try gasses, which would...and we tried other ways of phosphating those fibers by gas treatment, not only POCL treatment, there are other ways. But at this time I'm not sure that I could tell you which one, but there are other ways.

But the idea was to try...let's try to modify this without using the wet process, because you would have to remove the water and this costs money.

DR. UFFEN: Why phosphorous? Why not fluorene or something else? Is there some chemical, basic chemical characteristic that led you to the phosphorous?

THE WITNESS: Well, it had been observed in the literature that when you phosphate those fibers there are some technological advantages for the industry. When chrysotile is phosphated by whatever process, either wet or this new process, the

THE WITNESS: (cont'd.) drainage rate is very interesting. The drainage rate is decreased.

Are you familiar with this...?

DR. UFFEN: No, but I think I see the point. So the use of phosphorous had already been contemplated for other reasons, and it was a wet chemistry process?

THE WITNESS: Exactly.

DR. UFFEN: I understand why you...

THE WITNESS: Why go into the gas method.

DR. UFFEN: Would there be any interest in your group in using something like sodium?

THE WITNESS: Well, I must tell you that since we found that we could keep the useful technological properties of chrysotile by dry process, and altering the chemistry of it in such a way that one of the characterizing peaks which seem to be associated with biological activity, this gave a lot of ideas to a lot of my confreres who are now trying to gas the chrysotile with everything on the shelf.

But, of course, for obvious reasons they keep it for themselves until it could be disclosed with full protection.

MR. LASKIN: Q. In what way has it altered the chemical property? Has it done something to the magnesium content of chrysotile? What has it done?

THE WITNESS: A. No. That's part of the usefulness of this process. You could possibly leach out the magnesium by acid treatment, but you come to a point where there is so little magnesium on the fiber that this fiber is no longer technologically useful. So we thought that, well, let's put something onto the magnesium groups with their hydroxyl groups sticking on the periphery, and let's try to put phosphate groups onto these.

This apparently does the same kind of, produces the same kind of infrared spectrum as when you forcibly

A. (cont'd.) by milling introduce the same change. Namely, the disappearance of that peak at 1020.

Q. By coating the surface?

A. That's right.

Q. Rather than leaching out the magnesium with some acid solution?

A. That's right.

Q. You produce effectively the same result?

A. Mmm-hmm.

Q. I take it...

A. And again, and the processes by which you would leach are also wet processes. You have to dip these fibers into solutions, so people would like to get away from this wet process.

Q. Has your group itself done any research with asbestos and cement dust?

A. We are now doing this. We are now trying to do what, essentially what Deruyttere has done and has presented in 1980 in Torino, to examine more physiochemical parameters and more biological effects on the asbestos, has it been modified by introduction with cement.

Q. I looked at that article quickly, and there were two things that struck me about it. Number one, the asbestos-cement application was in fact an application that contained only ten percent asbestos and ninety percent cement. Second, that when you tagged on cement particles to the asbestos, of course you altered the diameter, you altered the diameter of the substance which may have affected its toxicity in terms of inhalation, and I'm just wondering whether you are looking at either of those issues and trying to correct for either of those issues, if indeed a correction needs to be made.

A. That's right. You are quite right in saying that possibly what might have happened during the process leading

A. (cont'd.) to asbestos cement that geometric as well as chemical characteristics might have been changed.

It's obvious that...well, it's obvious...he shows one chemical characteristic which has been changed. It could very well be that also geometric characteristics have been changed, but what he sees is that what he ...he runs this x-ray fluorescent spectrum, he says that when you compare the spectra of optically pure, virgin, the same type of fibers, optically they look very much the same, and yet that one is chemically different.

But optically, and therefore geometrically, I would assume, but he didn't go into the distribution of length and so on.

That's the type of thing that IRDA is trying to look for.

Q. I've only got a couple...really one other question.

I took it from something you said this morning that you were only looking at chrysotile yourself, for your research group?

A. Well, we must look at our...let's put it that way...of course chrysotile is the main interest, for obvious reasons - Quebec reasons, Canadian reasons. But also for another obvious reason - ninety percent of asbestos, the commercial variety which is used throughout the world, is chrysotile.

Q. My only question was, because I note a lot of the other...most of the other literature appears to concentrate on chrysotile. Is there some suggestion that there is something about chrysotile, as opposed to the amphiboles, that may lend itself more to this kind of alteration? Are the amphiboles less susceptible to the kinds of processes that you are researching right now than chrysotile might be?

A. I wouldn't say that. I wouldn't say that.

Q. It's a matter of economics?

A. It's entirely possible that one could look at the chemistry of, say crocidolite or amosite or anthophyllite, or what have you, tremolite, and possibly, by a totally different approach, chemically change these fibers and possibly alter their biological behaviour. It is possible. Theoretically I could, but of course we are more concerned with the ninety percent of the work production.

MR. LASKIN: Okay. Thanks very much, Dr. Dunnigan. Thank you, Mr. Chairman.

DR. DUPRE: Miss Jolley?

MR. LASKIN: I'm sorry, Mr. Chairman, just before we carry on, I forgot to introduce Mr. Shumacher who is here as Mr. McNamee's assistant this afternoon.

DR. DUPRE: You are welcome here.

CROSS-EXAMINATION BY MISS JOLLEY

Q. I'm a little confused in the whole discussion of the...

A. No wonder, my dear. We are all a bit.

Q. ...hemotoxic and cytotoxic experiments that you were talking about earlier this morning.

A. Yes.

Q. And the Langer material. Just in response to Mr. Laskin, did you say that crocidolite was nonhemotoxic, but cytotoxic?

A. Oh, no, no. I don't say it is non. I think it is less hemolytic.

Q. Hemolytic, right.

A. That's right. On a weight basis. If you were to take, say, in one experiment, given experiment, if you were to take on a weight basis of say ten micrograms or fifty micrograms of one category and fifty micrograms of another, it appears that

A. (cont'd.) chrysotile would produce in a quicker way the hemolysis than would crocidolite, but that applies only to the red blood system. Not to the macrophage system.

Q. Well, in the macrophage system then, what is the comparison?

A. Well, I don't have the figures, but it appears that it's far more complicated than the macrophage, all right, because we are dealing with a cell that has a nucleus and we are dealing with a situation where you have a sort of two-stage response...a first-stage response which is rather quick and which seems to be associated with the effect on the outer membrane of the macrophage, and then later on when you pursue your sampling of what leaches into the medium, you see that there is something else that goes. This comes...whereas the first phenomenon might occur very quickly, in terms of a few minutes, the other one might occur later on.

That's why we have people who are doing these experiments by incubation medium and they run these experiments for eighteen, twenty, twenty-four, thirty hours to make sure that they have the whole picture.

But this is further...I hope I'm not introducing more confusion than there is already in that field...all these comparisons between the chrysotile and crocidolite and so on, especially in the case of chrysotile, have been obtained by... have been obtained with samples which were prepared, and this is one point I would like to insist on, test samples which were prepared by methods which admittedly, now - not fifteen years ago, we didn't know anything about this at that time - but which now seem to be very harsh methods of producing short fibers, and there are a lot of people who have been using short fibers which were obtained by these harsh methods which were producing these chemical alterations, and now we begin to wonder - are these effects

A. (cont'd.) we observe, are these due to geometry only, or are they not due possibly also to chemical alteration which occurred in the process of preparing. That's why it's very hard to differentiate chrysotile and crocidolite on the basis of experiments done maybe fifteen years ago when...or maybe ten years ago...when these test fibers were produced by hand milling.

Q. But you are saying...I am confused because you said to us that crocidolite was cytotoxic.

A. Yes, on a macrophage.

Q. And in Langer's article, whichis tab eleven, on page 186, partially down the page there is a statement being made, and it's the...

A. What page did you say?

Q. Page 186, tab eleven.

DR. UFFEN: The second last paragraph.

MISS JOLLEY: Q. The second last paragraph, at the bottom. It says, "Whether these properties are related to fibrosis or carcinogenesis is purely speculative", which is the next question, but Allison, 1973, has noted that crocidolite, the blue color of which is due to charge transfer, has little cytotoxicity. And I'm confused.

A. Yes?

Q. Well, you have just told us that crocidolite is cytotoxic and now this says to me that it's not cytotoxic.

A. Well, in our hands it is cytotoxic, and I tell you more. In our hands, very short fibers, as Stanton said, are not very biologically interesting.

Q. They are...?

A. Cytotoxic. It depends on the way you are producing them. It depends on the way that you are achieving this population of short fibers.

Q. Okay. My next question is that...I mean, obviously you said to us earlier this morning that there is a

Q. (cont'd.) correlation between hemotoxic and cytotoxic and carcinogenesis, and fibrosis and carcinogenesis?

A. Yes.

Q. The reason why we are concerned about this is, obviously, ultimately...

A. Oh, what these people have said, and I was trying to remember and I'll make sure that I will send you a list of papers, rather recent, who are correlating both hemolytic activity and macrophage cytotoxicity to carcinogenicity.

Q. Well, if the ball-milled fibers were lower hemotoxic, they still did produce cancer in the experimental animals.

A. Where did you see that?

Q. Is the concern not that the biologically in vivo... the use of ball-milled fibers in the biological experiments was being criticized because those are not the fibers that are being used in general industry, but the animals still got cancer with ball-milled fibers?

A. Well, I read something different. Mr. Stanton said that there is a relationship between fiber size, and he says that when you have these...he says that the longer and thinner the fiber, the more carcinogenic it is.

So the opposite is, the shorter, they are less carcinogenic.

Q. But in the inhalation studies is it not true that the criticism of the inhalation studies has been because they were using these ball-milled fibers and they were not...am I reading more into this?

A. I would have to know which inhalation studies you are referring to, using ball-milled short fibers.

Q. I'll have to...I'm sorry, I'll have to drop that because I can't think offhand.

Q. (cont'd.) My next question has to do with - are you suggesting to us that the carcinogenic properties of asbestos are because they carry other carcinogens?

A. I am saying that there could be a very clear possibility - not from my own experience, but from what I read in reports which were presented to EPA sponsored studies, in which people tend to think that the, one of the potential reasons for some carcinogenic activity of some fibers, whether they are short or long, or modified or not, whatever, might be related to the fact that they may act as carriers of normally-circulating carcinogens in the environment.

What I'm suggesting is that if this model is a plausible model, a plausible explanation, then there are fibers which are carriers of, potential carriers of some other substances which may not be carcinogenic in itself per se, might carry carcinogens like tobacco smoke.

Q. But, I mean, the animal experiments, are they not in a controlled fashion that would...it's the fibers? They are not carrying?

A. That's right. You are quite right.

But I have never seen in animal inhalation experiments, if we want to go that fine of a precision, I have never seen people go and take the trouble of making sure that their test materials do not contain already carcinogens adsorbed on their fibers. That would be a tremendous work, but...

Q. The last question I have is from your conclusion of the statement that, page seven, your statement today, and that is that you are indicating, following your argument,

> "The regulations concerning the use by the consuming public of chemically altered chrysotile in the form...", etc,..."are not supported scientifically".

I am asking you, I mean surely you think that the

Q. (cont'd.) Commission is dealing with more than just the use of the final product? I mean, you are addressing one aspect of this Commission's...

A. Yes, this was quite clear this morning. I am addressing that part of the preoccupation of this Commission - the use of...end use.

Q. But there is native asbestos being used in Ontario?

A. It's possible. I don't know.

MISS JOLLEY: That's all I have. Thank you.

THE WITNESS: It's easier said than verified. My point is that if we are going to say that native, unaltered chrysotile is being used, one has to verify this, and there are ways to verify it.

You must not assume that. That's the point.

MISS JOLLEY: Thank you.

DR. DUPRE: Thank you, Miss Jolley.

Mr. Hardy?

MR. HARDY: Yes, sir.

CROSS-EXAMINATION BY MR. HARDY

Q. Dr. Dunnigan, I guess I would just like to make sure I understand the import of some of the things you have suggested to us today. We have heard over the summer a good deal of testimony that the dimensions of asbestos fibers in various fiber clouds at various points along the life cycle of asbestos may vary considerably, and that variance may be significant in terms of health effects.

A. Yes.

Q. It's true that what you are telling us is that similarly, the chemical structure of the fibers in different clouds in different parts of the production process may also vary, may also have an effect of biological significance?

A. Yes, and I say that this could occur concomitantly. Not only handling or, I don't know, manufacturing processes not only lead to a situation where you have various sizes of fibers in given situations, but at the same time the chemistry may be changed. Therefore, I say we should not assume that when we see under the microscope, optical microscope, something which looks like this and say well, this is a fiber - my question as a scientist is, what is it exactly, and therefore before reaching the conclusion that I have so many fibers of well-defined chemistry...I mean any experimenter would want to have chemically defined test materials before he is going to draw any conclusions whether these test materials are hormones, seroids or pesticides or what have you. He wants to have exactly what the chemistry of it is, and then give his own conclusions.

Q. In terms of one product, let's start with asbestos cement, I think you presented some evidence and discussed earlier the fact that asbestos-cement dust has at least one different chemical property from pure chrysotile asbestos?

A. Yes. This was disclosed at the Torino meeting.

Q. Right. Is the dust we are talking about here dust which would occur in fabrication of asbestos-cement pipe?

A. We have to be careful here because to my knowledge of the industry, little knowledge that I have, asbestos-cement sheets, plates, are made - to my knowledge - exclusively with chrysotile variety of asbestos, whereas pipes and certain pipes of a certain diameter, I am told, are made with chrysotile and something else - sometimes it's amosite, it could be crocidolite or what have you.

Then, it's very difficult to associate biological effect to one particular item in the whole hodgepodge that there is there.

Q. In the study that you presented today, was that

Q. (cont'd.) asbestos cement with crocidolite, that was pure...?

A. Pure chrysotile.

Q. Do you know whether work has been done analyzing asbestos-cement dust where crocidolite was included in the...?

A. Not to my knowledge. If you mean experimental studies?

Q. Or in the studies that characterized the chemistry of that dust in comparison to the pure...

A. No, not to my knowledge.

Q. With respect, back to the question I started with, the dust which was referred to in the study you discussed was dust created when the asbestos cement was cut, after the product was produced. Is that correct?

A. That is right.

Q. It was at that point that they clearly found a chemical difference?

A. Oh, yes. It's at this point in the manufacturing process where they have to grind holes or polish some corners...I don't know exactly...or make sleeves, or something like that - polishing or what have you. It's at this point, this is truly asbestos-cement dust and if you harvest the fibrous part of that dust and compare it with the original chrysotile, you see the difference.

Q. Has anyone, to your knowledge, tried to characterize the dust in an asbestos-cement pipe plant, which would be, as I would look at now, an intermediate stage between the pure fiber in the mine and the cement dust after the pipe is completed?

A. No. Not to my knowledge.

Q. So you don't know to what extent the fibers

Q. (cont'd.) in an A-C pipe plant might be chemically altered from the pure fiber?

A. We don't know to what extent and at what particular point it might be.

As you see, there is room for research.

Q. I gather from your discussion of the Wehner inhalation study with hamsters, which is in tab five, that you are suggesting that the biologic effects of asbestos-cement dust may be quite different from the biologic effects of pure chrysotile fibers?

A. Well, I am not suggesting it. That's their result.

Q. And that's...

A. In one study, which Dr. Mustard mentioned this morning, made in 1975, they were using pure, unaltered, chemically unaltered chrysotile, and they really dusted those hamsters five hours a day, five days a week for three, six and fifteen months, and at the end of this period they had successfully obtained asbestosis and started to get some real mess. They had succeeded.

When they repeated - the same people at the same research institute - the Battelle Institute - using the same species at the same dust exposure levels...at least this is what we read in that paper...there were none of them.

His hypothesis, because he did not know why this would happen, but it did happen, was that there might have been some chemical changes on the chrysotile that would explain why they were not observing the same results.

Q. I guess your further suggestion might be that for men working with asbestos-cement pipe in the field, that biological significance of the fibers there might be quite different from the biological significance for workers working with pure

Q. (cont'd.) chrysotile?

A. Well, yes. Because whatever may be emitted in handling of asbestos-cement sheets is not chrysotile anymore. It's a different chemical compound. It's...I don't know how I could...but it's something different.

Q. You didn't discuss this morning at all anything about what happens to chrysotile fibers during their use in friction products, in terms of do the fibers change in the production of friction products, or do they subsequently change in the use of the product in say a brake, which at some point may let off some dust, for instance, in a brake shop when the brakes are being replaced. Do we have any knowledge about chemical changes to chrysotile fibers in that whole friction product process?

A. Oh, yes. As you can see, in my presentation I said this may be illustrated by two cases. But I could have a third case, which would be another one, and we could possibly think of other cases. But this is very, very well known and there are a number of publications showing that brake linings containing chrysotile asbestos, when they are used, they are used as a friction material, of course, and the heat generated by the friction transforms the chrysotile into a completely different compound, which is forsterite, to the point where I think the figures are over ninety-nine percent of the dust which you could retrieve in the brake shop is forsterite, not chrysotile.

This is another example of what happens to chrysotile in end use, but I would be tempted to think that a chemical modification has occurred even before the friction and the heat is applied, because...

Q. What leads you to think that?

A. Well, the brake linings are formed with thermo-setting types of resins, phenolic resins or, you know, it's not

A. (cont'd.) just a simple cake of asbestos, of chrysotile asbestos. It is molded and baked into other compounds.

Q. So does that mean that even one percent of the dust from the brake, which is still chrysotile and not forsterite, might be chemically different from Canadian chrysotile?

A. It's certainly chemically bound to the other compounds which make up the final product which is a brake lining.

Q. Has anybody analyzed that fiber, or do we have any documented evidence of that?

A. There are some. This was, obviously, made in the U.S.A., reports to EPA, NIOSH, and also by the automotive industry.

Q. One other industry which uses a good bit of asbestos is the flooring industry, for backing for tile and vinylasbestos tiles. Do you know of any studies of chemical changes of chrysotile fibers in that process?

A. Not to my knowledge.

Again, if I may say so, this is precisely what IRDA is about to do. We have to make sure that whatever fibrous materials which might be emitted from finished products, end uses by the consuming public, is it chrysotile, is it transformed chrysotile, and what kind of a health hazard would it present.

But until such time, we can't tell.

I hope you will realize that those data that I have given you from...for instance, this one by Deruyttere, is quite fresh. It's Torino, 1980.

So more and more we are turning to examining what happens to the original components in end use or a finished product.

In other words, is it a simple agglomerate of, you know, of individual components which maintain their chemical integrity, or are they chemically transformed and a totally different compound altogether.

Q. Let me just see if I understand one other thing. We have been talking about alterations of chrysotile fibers which occur in the production process, and would it be fair to assume that at the beginning of the production process, the beginning of an A-C pipe lying in a factory, or the beginning of a...when the chrysotile fibers come into a friction products plant, that it's unlikely that any chemical alteration has occurred to the fibers at that point? As compared to, say the fibers in the mine?

Or is it possible that alterations may have even occurred in milling?

A. I don't think that there could be...I don't see any way in which it would be chemically altered before...at the beginning of the manufacturing process.

Q. Although we do know that with a good deal of mechanical work on the fibers, such as you have the ball-milling, there are chemical changes?

A. Oh, I see what you mean. In the process of... in the mills, producing the proper grade for the...

Q. Could that have a chemical effect on the fibers like ball-milling does, or has anyone looked at that, I guess, I shouldn't ask you to speculate?

A. I can only speculate though. But I don't think they are chemically altered.

DR. UFFEN: This prompts me, if I may, to ask, can you give, or has anybody given, an explanation as to why a physical process, ball-milling, produces a change in the chemical composition or structure? I can think of one, but I'm not sure it's a very good one and I'm wondering if there...

THE WITNESS: Well, the explanation that I was given by people who know about these things is that, for instance when you are dealing with ball-milling, that one process, you have a cylinder, essentially, in which you put your chrysotile or

THE WITNESS: (cont'd.) what have you, and this turns along an axis for minutes or hours or days, and inside you have these steel balls or ceramic balls, or what have you, and of course when...the explanation would be this...that when...I forget this now...when a steel ball would hit the bottom of the cylinder, at the point of impact there would be some tremendous energy which applied at one point, which would have an effect on the chemical binding on the atoms of that crystal.

DR. UFFEN: Would it produce a high temperature for a short time?

THE WITNESS: It could be temperature, it could be...I don't know.

But then if you have a large number of steel or ceramic balls turning for hours, on and on, you might reach a point where you can see, as Dr. Langer saw, first you have these three characterizing peaks, and after awhile you have this...you may still have something of a peak, and if you wait long enough then this is what you would have, you know, a gradual disappearance of that peak due to the repeated action of the...I don't know what would be your explanation.

DR. UFFEN: Well, it was essentially that, only I assumed that the transfer of energy you mentioned would result in a high temperature, and that you, right at that little place where the milling was actually taking place, for a brief instant you turned it into forsterite or theolite, which is the other end, and then it would come back again when the pressure was off.

That's just a slight variation. But if that kind of explanation is true, then any kind of manhandling of the fiber from the time they take it out of the stope until it gets into process, according to that kind of theory, would be open to both changes in physical shape and size, and chemical structure or composition.

THE WITNESS: You are right. Except that the industry who is milling that stops at one point where they have useful fibers. In other words, they crush and grind the ores and so on until such time as these are the length for technological purposes, that is obtained.

If they crush too much or for too long, they won't have any fibers. They would be so short that it would look like flour and lose much of its...

DR. UFFEN: One of the things that is probably going around in the backs of peoples' minds here, who have heard other witnesses, there's a whole bunch of small fibers that we can't even see, measure or detect, count or anything else with the present methods. They are too small, and these are presumably ones that have gone through a lot of this kind of process.

THE WITNESS: It could be. But if you were to obtain short fibers by other methods, which are so-called less harsh or soft methods like water fractionation, and you harvest very finely short fibers of a given range distribution which have not undergone that type of harsh treatment, you are still left with these characterizing peaks.

So handling certainly...the more you handle it, the more you mill it, goes into that. But at what point have you reached when you stop crushing and grinding these fibers in the industry, I wouldn't know. But I would presume that they are still like that.

DR. UFFEN: It seems such an obvious experiment for your sponsors or you to do, you know, quite frankly.

THE WITNESS: Quite correct.

DR. UFFEN: We'll recommend another two and a half million dollars.

THE WITNESS: Thank you very much, Dr. Uffen. My coming here was very fortunate.

MR. HARDY: Q. I just, I think, have one more question , but it may take a couple of questions to ask it, Dr. Dunnigan.

I just want to draw the distinction between... let's see if you agree, if I properly understand where your treatment process of fibers fits into what we have been talking about, and what we have been talking about up to this point is a number of things that happen to fibers through their normal life cycle, some of which may make them less biologically significant, and what you and your people have patented is a way of treating fibers very early in the process.

THE WITNESS: A. Yes.

Q. Which you believe may make them considerably less biologically significant than throughout the process. Is that a fair way to understand how it fits in?

A. That's right. That is right.

MR. HARDY: I don't have any further questions.

DR. DUPRE: Dr. Uffen?

DR. UFFEN: Well, just perhaps this should come from our medical man, but the question that follows from that is, have you given any thought to the possibility of treating existing asbestosis in a living animal? At the other end of the treatment instead of at the beginning?

THE WITNESS: No, we have not gone into that, sir. For a number of reasons. Well, the first one being the fact that well...we just started, literally. We are not back for twenty years, it's rather recent.

But I have heard in Cardiff, from Drs. Davies and Sherbling, who told me that the Japanese have come and seen them to study the possibility that they could use their chelating agents or what have you, in order to passivate whatever fibers might be present in the lungs of highly-exposed workers.

THE WITNESS: (cont'd.) But quite frankly, I am not a medical man and I couldn't...

DR. UFFEN: This is a slightly different kind of question. Are you free to tell us who is the owner of this patentable process? If we wish to pursue this further, to whom do we go? Are you free to tell us?

THE WITNESS: Yes.

DR. UFFEN: Who?

THE WITNESS: Le Societe National de l'Amiante... SNA.

DR. UFFEN: Thanks.

DR. DUPRE: Dr. Mustard?

DR. MUSTARD: I would like to come back to some questions that we were into this morning, and raise the problem of the need for a standardization of fiber mix, if I can use that term, in terms of dimension of fibers, and estimation of concentration of fibers when one is doing this experimental work, and I ask you the question as to what methodology is available to monitor not only using asbestos fibers, but other fiber systems that one might want to work with, ways of ensuring that the mix of fibers that you are using, no matter what the treatment you expose the fibers to, that portion is the same.

The problem is, it would seem to me in looking at what is going on, you have to hope that when you start with a sample of fibers and modify it, that that sample in terms of the mix and size doesn't change on you.

THE WITNESS: Quite right.

DR. MUSTARD: Is there anything developed at all of ways of ensuring standardization of materials that are being used, or do you rely totally on morphological estimates?

THE WITNESS: At the present time, this is what most people are doing. We are relying on morphological estimates

THE WITNESS: (cont'd.) by counting one by one the number of fibers and making blank distributions.

DR. MUSTARD: And diameter distributions?

THE WITNESS: And diameter distributions. And there is no...well, I would hope that there would be some magical blackbox in which you would put these samples and come out, but you have to do it manually.

I know that there are some apparatus which are being developed by Vickers Company, I think it is, in Manchester, to try and have some automatic - not only counting of particles, but estimation of the aspect ratio, and process this into a micro-computer which would be able to read, you know, just from an image.

DR. MUSTARD: The second question tied into this area is.... the dispersment of fibers outside the body, or body fluids, may be different than when they are put within a body compartment. Do you have any information about what the modification of the surface does on the tendency of fibers to aggregate in a variety of circumstances - such as if you change Ph, you change ionic strength, you change protein concentrations in which the fibers would normally be bathed?

THE WITNESS: We haven't done experiments on that particular aspect, in other words, what happens to these fibers once they are modified, how would they react with slight changes in osmolarity of biological fluids, Ph, and what have you. This is your question. We haven't done that.

DR. MUSTARD: That brings me to my third question. One of the uses of asbestos fibers have been involved, of course, in weaving a form of fabric from asbestos. Have you given thought, or has anybody tried to make asbestos fabrics...you can make them of quite reasonably small, thin dimensions..and then modify the surface of that fabric and then studied the macrophage

DR. MUSTARD: (cont'd.) with the surface?

The reason for raising the question is, it seems to me you could have a fairly standardized surface...

THE WITNESS: A solid state type of...

DR. MUSTARD: Yes, but you then modify that surface and look at your macrophage interaction, which would get around a lot of these other problems. Has anybody tried to do that?

THE WITNESS: Not to my knowledge. Nothing has been published on that, to my knowledge. But I think we would... although the idea in theory is very exciting, I think it would be very difficult to interpret the results because when you have macrophages, you have harvested them after bronchoalveolar lavage, and there are some behavioural aspects of those cells once they are kept outside their natural environment and one of them is their ability to become attached to or not attached to, and I think it would be...although I would agree that it is very exciting to try and see what would happen if one were to modify the solid state sheets, what you would call sheets of untreated or treated asbestos, I wonder...I don't think I would be qualified to interpret the results that would result from that.

DR. MUSTARD: Well, if we go to tab nine, pages 752 and 753...I think I've got the right place...there are macrophages placed in a medium...

THE WITNESS: Excuse me. Where was that?

DR. MUSTARD: Pages 752 and 753 of tab nine.

Your macrophages are placed in a medium containing a balanced salt solution, if I may use that term, which in tissue culture work is essentially a physiological solution...I'll just make...

THE WITNESS: Hank's medium. Yes.

DR. MUSTARD: I'll just make a digression for a moment. One of the things that one learns in life, indeed it

DR. MUSTARD: (cont'd.) was a Dr. Parker at the Connaught Labs in Toronto who established this point in tissue culture work many years ago...that cells do not like living in media that is remote from what they normally would be happy with inside the human body, and one of his rules was thou shalt never put a cell, if you want it to be normal, in a salt solution. You put it into a proper tissue culture medium.

But the problem with the red cell is that you can put it in anything because it doesn't tell you whether it's alive or not, but your macrophage does. Of course, the suspending medium, you admit, in these two experimental protocols is radically different: One is water with a Veronal buffer in it, which bears no relationship to the salt solution, and here you will follow the dictum that you use a tissue culture medium so the cells will be alive.

THE WITNESS: But the same thing can be said with all tissue culture studies.

DR. MUSTARD: Yes, but at least it's a proper physiological medium, it's an important point.

Secondly, you have in that medium calf serum...I guess that's referred to on page 754...and what I am coming to is, I believe that you are looking at cell/surface interactions the presence or absence of serum can be of great importance.

THE WITNESS: Yes, very much so.

DR. MUSTARD: Do you get this reaction if the serum is left out of the medium?

THE WITNESS: The reason why the serum must be added is because it is felt that if you want to try and get as close as possible to the situation which is found in the in vivo environment, you have to realize that those fibers are coated with some body fluid proteins, and therefore you try to mimic, to put these fibers as close as possible as the situation

THE WITNESS: (cont'd.) would arise in the in vivo situation.

DR. MUSTARD: I could then make the argument - wouldn't that have been a logical point to have put in terms of the hemolysis studies as well, that indeed the hemolysis studies should have been done in a medium containing the normal protein composition?

THE WITNESS: Yes, but the red blood cell coming from, their natural milieu is serum. These cells are not washed clear of the serum proteins. They already have their own. They are, so to speak, contaminated with serum protein already.

DR. MUSTARD: I'm not sure I would agree with that, but that's not the point.

I guess my question is, the reason I'm asking the question about the serum is that most cell surface adherence studies, the macrophages would be called, in the jargon of the trade, white cells, show very pronounced difference in their reaction to surfaces whether or not the proteins that are normally in place are present. This indicated to me you ought to have them there.

My reason for asking about the flat surface is that there is a group of plasma proteins in the complement field, and there is very good evidence that absorption of complement onto the surface is a very important trigger in what happens to cells like macrophages when they interact with surfaces.

My reason for asking the question was that it would be interesting if your cytotoxicity studies were less dramatic in the absence of serum.

THE WITNESS: The absence of serum?

DR. MUSTARD: Yes.

THE WITNESS: And on a solid state?

DR. MUSTARD: Well, in your system as it is, if

DR. MUSTARD: (cont'd.) they were less dramatic.

It's obvious it hasn't been done, but if you found that that was so, you could then go to your solid state surface very easily because there's whole vast field in the complement field which...how you induce cell injury and damage that you are studying here with the macrophages, which is related to surface absorption properties.

THE WITNESS: Thank you.

DR. MUSTARD: You've answered the question. It seems to me it's an intriguing thing to do, to know the wetter, if I may use that term, try and look at adherence studies or not.

Finally, in the experiments which you have done on hemolysis, you reported the story of fibers and phospholipids that you got some protection in the hemolysis of the asbestos fibers. Has anybody done the experiments in the presence of albumen?

THE WITNESS: Not to my knowledge.

DR. MUSTARD: I see. I'm just curious, because that also provides...

THE WITNESS: Inhibition of...

DR. MUSTARD: Inhibition of reaction.

THE WITNESS: I would have to read through again Bignon's article. If he had not...he has not mentioned that as a possibility, but I would have...but I don't recall.

DR. MUSTARD: That's all I have, Mr. Chairman.

DR. DUPRE: M. Casgrain, do you have any final questions of your witness?

M. CASGRAIN: No, sir.

DR. DUPRE: Well, may I on behalf of all of us thank you most warmly. Merci et bon voyage.

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THE INQUIRY ADJOURNED

THE FOREGOING WAS PREPARED FROM THE TAPED RECORDINGS OF THE INQUIRY PROCEEDINGS

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